

Platelet-Rich Plasma (PRP) for Knee Osteoarthritis Technology Overview

Technology Overview

Disclaimer: This Technology Overview was prepared using systematic review methodology and summarizes the findings of studies published as of August 25, 2021, on the use of platelet rich plasma for the treatment of knee osteoarthritis. As a summary, this document does not make recommendations for or against the use of platelet rich plasma. It should not be construed as an official position of the American Academy of Orthopaedic Surgeons. Readers are encouraged to consider the information presented in this document and reach their own conclusions about platelet rich plasma for the treatment of knee osteoarthritis.

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Platelet-Rich Plasma Data Summary

Introduction

Platelet-Rich Plasma (PRP) is a concentrate of platelets and plasma proteins derived from a patient's blood, which is used to deliver high levels of platelet-associated growth factors and bioactive molecules in the treatment of diseases, including osteoarthritis. There have been multiple clinical studies evaluating the safety and efficacy of PRP in the treatment of osteoarthritis, including randomized controlled trials comparing the results of PRP with other injectable treatments, most commonly hyaluronic acid. In this Technology Overview, we assessed the literature that addressed the following question: When patients are treated for osteoarthritis of the knee using PRP, are the outcomes of that treatment different from a comparison group (alternative treatment, placebo or no treatment)?

Summary of Findings

PRP versus Placebo

There were eight high quality studies (Lin 2019, Gormeli 2017, Wu 2018, Patel 2013, Ghai 2019, Qamar 2021, Elik 2020, Smith 2016) and one moderate study (Eroglu 2016) evaluating PRP vs placebo saline injections for patients with osteoarthritis of the knee. The high-quality studies evaluated outcomes in a total of 433 patients (total patients in both the PRP and saline groups).

In general, PRP showed an improvement in patient reported outcomes (PROs) including total WOMAC scores in all six high quality studies which reported WOMAC (Lin 2019, Wu 2018, Patel 2013, Ghai 2019, Elik 2020, Smith 2016) and VAS pain scale scores (Pate; 2013, Ghai 2019, Qamar 2021 and Elik 2020). No statistically significant improvement was reported in the moderate quality study (Eroglu 2016). PRP also demonstrated a benefit over placebo for PROs related to knee function, although in fewer studies, including an improvement in IKDC in two high quality studies (Lin 2019, Gormeli 2017) and WOMAC Function/Stiffness in five high quality studies (Wu 2018, Patel 2013, Ghai 2019, Elik 2020, Smith 2016). No statistically significant improvement on WOMAC Function/Stiffness was reported in one moderate quality study (Eroglu 2016).

PRP was not found to have any significant effect on cartilage thickness using ultrasound evaluation (Elik 2020), or knee strength (Wu 2018).

In summary, PRP compared to a saline placebo treatment resulted in improved patient reported outcomes, with the primary improvements noted for questions relating to pain and stiffness reports, rather than reports of functional improvement. There was no evidence of cartilage structural improvement or improvement in knee strength in the single studies addressing those hypotheses. Moreover, the available studies documented rather small cohorts of patients, with products used and results presenting large variability. Thus, while this literature search reported results which seem overall in favor of PRP, each product remains weakly supported by heterogeneous data on small patient cohorts. More studies on larger patient cohorts are advised to confirm these findings and identify the optimal preparation and patient populations for treatment.

PRP versus Hyaluronic Acid (HA)

There were 18 high quality studies and seven moderate quality studies evaluating PRP vs hyaluronic acid (HA) injections for patients with osteoarthritis of the knee (Ahmad 2018, Bansal 2021, Buendia-Lopez 2018, Cole 2017, Di Martino 2019, Gormeli 2017, Lin 2019, Lisi 2018, Louis 2018, Montanez-Heredia 2016, Park 2021, Raeissadat 2020, Raeissadat 2021, Raeissadat 2015, Sánchez 2012, Tavassoli 2019, Vaquerizo 2013, Xu 2021, Basnaev 2021, Cerza 2012, Duymus 2017, Huang 2019, Raeissadat 2017, Spakova 2012, and Su 2018). The 18 high quality studies evaluated outcomes in a total of 1,777 patients (total patients in both the PRP and HA groups).

PRP showed more improvement than HA in patient reported outcomes (PROs), including total WOMAC scores, in nine out of 12 high quality studies that reported that measure (Bansal 2021, Buendia-Lopez 2018, Lin 2019, Park 2021, Raeissadat 2020, Raeissadat 2021, Raeissadat 2015, Tavassoli 2019, Vaquerizo 2013); however, three high quality studies found no difference between the PRP and HA groups (Lisi, Sanchez, Louis).

Patients treated with PRP also had improved VAS pain scale scores in six out of nine high quality studies reporting that measure (Cole 2017, Ahmad 2018, Tavassoll 2019, Raeissadat 2020, Buendia-Lopez 2018, Raeissadt 2021); two of nine high quality studies reporting the VAS pain score showed no statistically significant difference between PRP and HA (Lisi, 2018, Louis 2018), while the final study found worse VAS pain scores in PRP than in patients treated with HA (Park 2021). PRP also demonstrated a benefit over HA for PROs related to knee function, including an improvement in IKDC in six of six high quality studies that measured this outcome (Cole 2017, Lin 2019, Ahmad 2018, Gormeli 2017, Park 2021, Bansal 2021) and better WOMAC Function subscores in eight of ten high quality studies where that was reported (Raeissadat 2015, Tavassoli 2019, Raeissadat 2020, Buendia-Lopez 2018, Vaquerizo 2013, Park 2021, Bansal 2021); two high quality studies showed no statistically significant difference in WOMAC Function subscores (Sanchez 2012, Louis 2018).

Only four high quality and two moderate quality studies reported on adverse events after PRP or HA injection (Ahmad, Vaquerizo, Park, Xu, for high quality, and Huang, Raeissadat 2017 for moderate quality). The three high quality studies that found differences in adverse events between PRP and HA also had mixed findings. One study compared the efficacy of single PRP vs HA using ultrasonographic assessment for synovial hypertrophy, synovial vascularity, and knee effusion at six months (Ahmad 2018). Their results suggested that patients treated with PRP had significantly less synovial vascularity, synovial hypertrophy, and knee effusions. However, another study reported increased rates of minor complications due to injection with PRP (Raeissant 2020) and a third study found an increased incidence of pain after injection (Xu 2021).

In summary, PRP compared to HA resulted in improved patient reported outcomes in the majority of high quality studies. It is possible that there are PRP or patient features that dictate who might do well with PRP treatment and explain the heterogenous and sometime contradictory findings, and further work to document those treatment and recipient characteristics are needed.

PRP versus exercise

There were four high quality studies (Rayegani, 2014, Elgandy, 2020, Raeissadt, 2020, Akan, 2018) and one moderate quality study (Gaballa, 2019) that met the inclusion criteria and compared PRP to exercise for patients with osteoarthritis of the knee. The four high quality studies evaluated outcomes in a total of 201 patients (total patients in both the PRP and HA groups).

PRP showed statistically significant improvement in outcomes compared to exercise for WOMAC in one study (Elgandy 2020), for SF-36 scores in one study (Rayegani 2014), for WOMAC Function-related patient reported outcomes in one study (Gaballa 2019), and for VAS Pain scores in one study (Elgandy 2020, Gaballa 2019), while, three studies reported no statistical difference in WOMAC Function/Stiffness patient reported outcomes (Rayegani, 2014, Raeissadat 2020, Akan 2018), and two studies reported no difference in WOMAC Pain scores (Rayegani, 2014, Raeissadat 2020) when PRP was compared with exercise. In one high quality study, PRP resulted in statistically significantly better WOMAC pain scores at six months after treatment (Akan 2018).

In summary, while there were some studies that reported better patient reported outcomes with PRP when compared to exercise, there were also studies that reported no significant difference after PRP injection when compared to exercise. Additional research comparing the use of PRP and exercise therapy, as well as their combination, may yield more clarity.

PRP versus Corticosteroids

There were six high quality studies (Elksnins-Finogejevs 2020, Forogh 2016, Joshi Jubert 2017, Khan 2018, Nabi 2018, Uslu Guvendi 2018) and two moderate quality studies (Huang 2019, Phul 2018) evaluating PRP vs corticosteroid (CS) for patients with osteoarthritis of the knee. The six high quality studies evaluated outcomes in a total of 359 patients (total patients in both the PRP and CS groups).

PRP showed inconsistent outcomes when compared to corticosteroids for VAS Pain, with a statistically significant improvement in four studies (Elksnins-Finogejevs 2020, Forogh 2016, Uslu Guvendi 2018, Phul 2018), no statistically significant difference in outcomes in three studies (Joshi Jubert 2017, Nabi 2018, Huang 2019), and statistically significantly worse outcomes in one study (Khan 2018).

Three studies analyzing WOMAC patient reported outcomes after injection with either PRP or CS also had varied results. One high quality study identified no statistically significant differences in pain, stiffness, or function WOMAC scores from baseline at six-months after injection (Khan (2018)). Another high quality study comparing triple- and single-dose PRP to corticosteroid at six

months after injection reported that the PRP cohorts had greater improvements in all WOMAC total, pain, stiffness, and function scores (Uslu Güvendi (2018)). One moderate quality study compared PRP to corticosteroid as well as HA and demonstrated significant differences in the PRP group in total WOMAC scores from baseline at 12 months after injection (Huang 2019).

Of the studies included in this comparison, only seven recorded body mass index (BMI), and of these, four (57%) recorded mean BMIs < 30 kilograms/meters². Current literature demonstrates that joint arthroplasty patients tend to be obese (BMI > 30 kilograms/meters²) (Fryar 2013, Raphael 2013, Changulani 2008, Liu 2021). Additionally, 25% (two out of eight) of the studies included severe Kellgren-Lawrence grade IV degenerative joint disease, (Kohn 2016) a class not presently recommended for administration of biologic therapies by the American Association of Hip and Knee Surgeons (AAHKS). These factors may influence the generalizability of the findings.

In summary, when PRP was compared to CS injection, there were varied results in patient reported outcome measures. Further randomized control trials are needed to optimize and standardize PRP preparations, with advanced imaging at longer term follow to determine any sustained effects of PRP injections.

PRP versus other drugs – NSAIDs, celecoxib, acetaminophen

There were two high quality studies (Heredia 2016, Buendia-Lopez 2018) and three moderate quality studies (Simental-Mendia 2016, Ayeni 2019, Reyes-Sosa 2020) that met the inclusion criteria and compared PRP to non-steroidal anti-inflammatory medications (NSAID) or acetaminophen for patients with osteoarthritis of the knee. The two high quality studies evaluated outcomes in a total of 119 patients (total patients in both the PRP and comparison groups).

PRP showed statistically significant improvement compared to NSAIDs/acetaminophen for VAS pain in all four studies that reported this (Buendia-Lopez 2018, Ayeni 2019, Reyes-Sosa 2020, Simental-Mendia 2016). WOMAC composite scores were also better for PRP than NSAIDs/acetaminophen in the two studies that measured them (Simental-Mendia 2016, Reyes-Sosa 2020). WOMAC patient reported outcomes relating to knee function were also better with PRP at 6 months (Ayeni 2019) and 3, 6, and 12 months (Reyes-Sosa 2020) in the two studies that reported this.

Collectively, PRP showed statistically significant improvement in several patient reported outcomes when compared to oral NSAIDs (three studies) or acetaminophen for patients with osteoarthritis of the knee. However, consideration should also be given to the limited sample size, blinding strategies, and small number of published studies which met the inclusion criteria. Additional research comparing the use of PRP and NSAIDs or acetaminophen may yield more clarity.

PRP versus ozone

One high quality study (Raeissadat 2021) and two moderate quality studies (Gaballa 2019, Duymus 2017) met the inclusion criteria and compared PRP to ozone treatment for patients with osteoarthritis of the knee. The high-quality study evaluated outcomes in a total of 119 patients (total patients in both the PRP and ozone groups).

In the one high quality study comparing these two treatments (Raeissadat 2021) PRP had significantly improved VAS scores at 12 months after injection. In the two moderate quality studies, PRP had significantly better VAS scores at three months (Gaballa 2019) and at time points up to 12 months after injection (Dymus 2017).

In the high-quality study comparing these two treatments (Raeissadat 2021) PRP had significantly better WOMAC pain, stiffness and function scores at 12 months after injection. Both moderate quality studies reported improved outcomes for PRP for WOMAC functional scores.

In summary, the few data available comparing PRP and ozone are in favor of PRP, with ozone offering short-term benefits that dissipate quickly while PRP presents longer lasting results.

PRP versus prolotherapy

One high quality study (Rahimzadeh 2018) and one moderate quality study (Eroglu 2016) met the inclusion criteria and compared PRP to prolotherapy for patients with osteoarthritis of the knee. These two studies evaluated 102 patients in total (PRP and prolotherapy groups).

In the high-quality study, PRP showed statistically significant improvement in outcomes compared to prolotherapy for WOMAC (composite, function, stiffness, and pain subscales) (Rahimzadeh 2018) and no statistically significant differences in outcomes in one moderate quality study (Eroglu 2016) on the same WOMAC composite score and subscales.

In summary, there is insufficient evidence to clearly support the superiority of PRP or prolotherapy in the treatment of OA of the knee. Further randomized controlled studies could be useful to establish PRP or prolotherapy superiority.

PRP versus Bone Marrow Concentrate (BMC)

One moderate quality study (Anz 2020) met the inclusion criteria and compared PRP to Bone Marrow Aspirate Concentrate (BMC) for patients with osteoarthritis of the knee. This study evaluated a total of 90 patient in the PRP and BMC groups combined.

This study showed no statistically significant difference in outcomes in WOMAC patient reported outcomes (composite and function/stiffness subscales), or IKDC. The PRP group did, however, score statistically significantly better than the BMC group for WOMAC Pain. Given the limitation of a single study and lack of statistically significant outcomes, it is inconclusive if PRP provides better results than BMC for knee OA or vice versa. Additional research comparing the use of PRP and BMC may yield more clarity.

PRP versus Autologous Conditioned Serum (ACS)

One moderate quality study (Pishgahi 2020) met the inclusion criteria and compared PRP to autologous conditioned serum (ACS). This moderate quality study evaluated outcomes in a total of 62 patients (total patients in both the PRP and ACS groups). In a randomized trial (Pishgahi 2020), two injections of either PRP or ACS were given one week apart, with a third arm consisting of prolotherapy. There were no significant differences between the PRP or ACS treatments in WOMAC or IKDC patient reported outcomes at one or six months; however, the ACS group had a lower (improved) VAS pain score than the PRP group at six months after injection.

Benefits & Harms

There were no significant harms reported from this intervention compared to other treatment modalities. Overall, the literature supports the hypothesis that PRP can offer statistically significantly greater benefit compared to placebo and active treatment alternatives such as HA, corticosteroid, and NSAIDs for patient reported outcomes related to pain and symptoms for time points up to 12 months. However, the optimal preparation and products for patients with knee OA and the extent of the benefit of PRP in terms of clinically important difference remain to be determined.

Important/Priority Outcomes

Pain, Validated Patient Reported Outcomes, Quality of Life Measures.

Cost Effectiveness/Resource Utilization

No studies looked at cost-effectiveness. Clouding this is the issue that while PRP is typically an out-of-pocket expense for patients, while other treatment modalities (HA, corticosteroids) may be covered by insurance. This may be one reason why we did not identify studies addressing this question. Similarly, with respect to NSAIDs and/or Acetaminophen, while it appears that PRP may offer some benefits in terms of patient reported outcomes of pain, there is no direct cost-benefit comparison in the literature to support or reject the significantly higher cost of PRP.

Acceptability

Platelet Rich Plasma (PRP) is commonly accepted as a safe biologic due to its autologous nature and the ease of preparation from venipuncture.

Feasibility

There are almost no limits to the feasibility of using PRP for knee osteoarthritis in the clinic or operating room setting as venipuncture is usually performed without any difficulty or risk. PRP preparation is primarily performed using FDA-approved centrifugation systems and kits provided by commercial entities. Injection of the final PRP preparation into the knee joint is a routine procedure performed in the office or operating room (OR) setting and will not limit feasibility.

Conflicts of Interest

Reference	Potential Financial Conflicts of Interest
Anz, A. W., 2020	One or more of the authors has declared the following potential conflict of interest or source of funding: The Andrews Research & Education Foundation received funding and material support from EmCyte to support this study. A.W.A. has received educational and research support from Arthrex and CGGMedical; consulting fees from Arthrex, Bioventus, Ceterix, MicroAire, and Blue Belt Technologies; speaking fees from Arthrex and Smith & Nephew; royalties from Arthrex; and hospitality payments from Procedural Orthopedics. P.A.E. is employed by EmCyte. J.R.A. has received speaking fees from Arthrex and Halyard Health; has received consulting fees from Theralase Technologies, Bauerfeind, and Physiotherapy Associates/Select Medical; and has stock/stock options in FastHealth, Patient Connection, Connective Orthopaedics, and Contessa Health. J.G.H. has received consulting fees from Carticept Medical, Fujifilm SonoSite, and Ferring Pharmaceuticals; speaking fees from Ferring Pharmaceuticals; honoraria from Tenex Health, Avanos Medical, and FidiaPharma; and educational support from Tenex Health. AOSSM checks author disclosures against the Open Payments Database (OPD).
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Future Research

The current literature suggests that PRP may have more benefit than placebo for improvement of pain and patient reported outcomes related to symptoms, for time points up to one year after injection. However, whether PRP can improve the structure or functioning of the osteoarthritic joint remains unclear. Additional high quality, double-blinded, prospectively designed randomized controlled trials, evaluating the efficacy of PRP against other non-operative treatments (placebo, cortisone, HA, physical therapy, and NSAIDs) evaluating both the efficacy of treatments for structural and functional outcomes and including subgroup analyses (e.g., OA severity) would be useful in bringing more clarity to the field. Functional outcomes could include measures of knee range of motion, strength, and walking ability. Structural changes could be measured using imaging changes from baseline. Collecting and reporting long-term outcomes (clinical and radiological patient data) would also be beneficial to contribute to the understanding of PRP's efficacy.

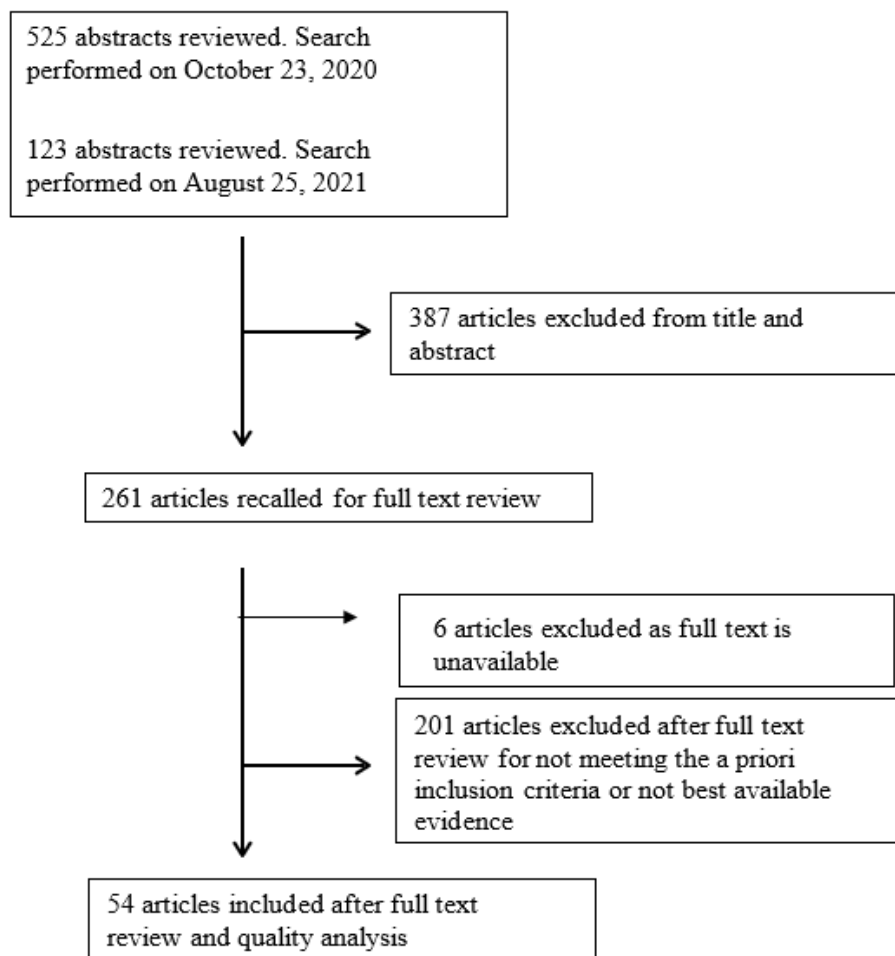
In addition to clear descriptions of patient demographics and severity of disease, future research should consider including leukocyte and/or platelet count data. This, as well as other important data (Kon, 2020) could make PRP factors comparable across studies. The PRP used should at least be classified as leukocyte rich (neutrophil or WBC concentration at baseline or above, or by the system used to make the PRP) or leukocyte poor (neutrophil or WBC concentration below baseline, or by the system used to make the PRP). Platelet count could be reported both as an absolute number and multiple of baseline platelet count.

Ultimately, both the quantity and quality of research being conducted and published addressing the use of PRP for knee OA is rapidly growing, with additional studies bringing better scientific understanding on a near-monthly basis. Some studies (example: Bennell 2021) were published after this project's final updated literature search and unfortunately could not be included directly in the analysis but are a testament to the rapid pace of research and may change clinicians' understanding of the field. They also underline the heterogeneity of the products and of the related study findings, which warrants stronger evidence with high level studies to evaluate the potential of each proposed PRP product.

Conclusions

The use of platelet-rich plasma (PRP) for the treatment of osteoarthritis of the knee has demonstrated statistically significant improvement in some patient reported outcomes when compared to placebo. When compared to multiple alternative treatments, the results varied. However, the current state of published literature also includes substantial limitations, including few studies evaluating knee function or structural change, and inconsistent reporting of leukocyte and platelet concentrations. Future higher quality research will be necessary to identify the efficacy of PRP (and the best PRP formulation and need for repeat dosing for symptom control) in providing long-term pain relief or improving the structure or function of the osteoarthritic knee.

Study of Attrition Flow Chart



Included Study Demographics

Author	OA Inclusion	White Blood Cell Information	Injections
Ahmad 2018	KL 1-3	Not leucocyte-free	3
Akan 2018	KL 4	Platelet yield: 6.36 ± 1.86	3
Angoorani 2015	KL 1-3	platelet count of at least 3 times comparing to the baseline	2
Anz 2020	KL 1-3	Leukocyte-rich	1
Ayeni 2019	KL 1-2	Not reported	3
Bansal 2021	KL 1-3	Leukocyte count: 0; Platelet count: $12.68-16.2 \times 10^5$ platelet/uL	1
Basnaev 2021	KL 3	PRP platelet concentration: $800 \times 10^9/L$	4
Buendia-Lopez 2018	KL 1-2	Leukocyte-poor	1
Cerza 2012	KL 1-3	Not reported	4
Cole 2017	KL 1-3	Leukocyte-poor	3
Di Martino 2019	KL 1-3	Leukocyte-rich	3
Duymus 2017	KL 2-3	Ycellbio kit	2
Elawamy 2021	KL 3-4	Not reported	1
Elgendy 2020	KL 2-3	Not reported	1
Elik 2020	KL 1-3	leukocyte count approximately as high as the number of leukocytes in the patient's blood ((1.0x)	3
Elksnins-Finogejevs 2020	KL 2-3	Hy-Tissue PRP® system	1
EROGLU 2016	KL 1-3	Leukocytes with a mean concentration of 1.2 ± 0.6 times with respect to the normal blood value, number of platelets per milliliter increased by means of 4.5 ± 1.3 times with respect to baseline blood values	3
Forogh 2016	KL 2-3	Concentration of platelets > 4x that of whole blood	1
Gaballa 2019	KL 1-3	Not reported	1
Ghai 2019	KL 1-2	Leukocyte-free	1
Gormeli 2017	KL 1-3	Not reported	3
Huang 2019	KL 1-2	Leukocyte-poor	1
Joshi Jubert 2017	KL 3-4	leukocyte-reduced	1
Khan 2018	KL 2	Not reported	1
Lin 2019	Ahlbäck OA stage IV	Leukocyte-poor	3
Lisi 2018	Shahriare e 2-3	Not reported	3
Louis 2018	KL 2-4	Leukocyte concentration: 0.86 ± 1.24	1
Montanez-Heredia 2016	KL 1-3	Leukocyte-weak	1
Nabi 2018	KL 2-3	4- to 6-fold increase in platelet count	3
Park 2021	KA 1-3	PRP platelet count: 976,000 uL; 3x whole blood	1
Patel 2013	Ahlback 1-2	Leukocyte count: 0, Platelet count: $310.14 \times 10^3/mL$	1 or 2
Phul 2018	KL 2-4	"Contains leukocytes"	2
Pishgahi 2020	KL 2-4	lowest leukocyte	2
Qamar 2021	KL 2-4	Not reported	3

Raeissadat 2020	KL 2-3	no platelet or WBCs was found	2
Raeissadat 2021	KA 2-3	PRP platelet concentration 4-6x	2
Raeissadat 2020	KL 1-3	Leukocyte-rich and platelet concentrations were 4–6 times normal	2
Raeissadat 2017	KL 2-3	Not reported	3
Raeissadat 2015	KL 1-4	Leukocyte-rich PRP and platelet concentrations 5.2 ± 1.50 times and 4.8 ± 1.80 times the baseline values in the first and second preparations	2
Rahimzadeh 2018	KL 1-2	Not reported	2
Rayegani 2014	KL 1-4	Leukocyte-rich	2
Reyes-Sosa 2020	KL 2-3	Without leukocytes	2
Sánchez 2012	Ahlback 1-3	Attempted to avoid picking up leukocytes	3
Simental-Mendia 2016	KL 1-2	Leukocyte-poor	3
Smith 2016	KL 2-3	Leukocyte-poor	3
Spakova 2012	KL 1-3	Not reported	3
Su 2018	KL 2-3	Leukocyte-containing	2
Tavassoli 2019	Ahlback 1-2	Not reported	1
Uslu Guvendi 2018	KL 3	WBC: 8.67×10^9 L	3
Vaquerizo 2013	KL 2-4	Attempted to avoid picking up leukocytes	3
Wu 2018	KL 1-2	Leukocyte-rich	1
Xu 2021	KL 2-3	leukocyte-poor	3

Summary of Findings Tables

SOF: PRP vs. Control/Placebo

	High							Moderate	
	Lin, 2019	Gormeli, 2017	Wu, 2018	Patel, 2013	Ghai, B. 2019	Qamar, 2021	Elik, H. 2020	Smith, P. A. 2016	Eroglu, 2016
<p>↑ Better Outcomes</p> <p>↓ Worse Outcomes</p> <p>● Not Significant</p>									
Composite									
WOMAC Total	↑		↑	↑	↑		↑	↑	●
Function									
IKDC	↑	↑							
WOMAC Function			↑	↑	↑		↑	↑	●
WOMAC Stiffness			↑	↑	↑		↑	↑	●
Pain									
VAS Pain score				↑	↑	↑			
WOMAC Pain			↑	↑	↑		↑	↑	●
EQ Pain		↑							

SOF: PRP vs. Acetaminophen

	Moderate
	Simental-Mendia,2016
<p>↑ Better Outcomes</p> <p>↓ Worse Outcomes</p> <p>● Not Significant</p>	
Composite	
WOMAC Total	↑
Function	
VAS Stiffness	↑
VAS Functional Capacity	↑
Pain	
VAS Pain score	↑
QOL	
SF Mean Physical Component	↑
SF Mean Mental Component	↑
QOL Score	↑

SOF: PRP vs. NSAID

	High		Moderate	
	Heredia, 2016	Buendia-Lopez, 2018	Ayeni, 2019	Reyes-Sosa, 2020
↑ Better Outcomes ↓ Worse Outcomes ● Not Significant				
Composite				
WOMAC Total				↑
Function				
WOMAC Function			↑	↑
WOMAC Stiffness				↑
WOMAC Function, 20% Decrease		↑		
WOMAC Stiffness, 20% Decrease		↑		
Pain				
VAS Pain score		↑	↑	↑
WOMAC Pain				↑
EUROQOL Pain Scale-Improvement	●			
EUROQOL Pain Scale- Worsening	●			
EUROQOL Pain Scale- Similar	●			
WOMAC Pain, 20% Decrease		↑		
EUROQOL Pain Scale-Improvement	↑			
EUROQOL Pain Scale- Worsening	↓			
EUROQOL Pain Scale- Similar	●			

SOF: PRP vs. Corticosteroid

Composite/Function

	High						Moderate	
	Forogh, 2016	Guvendi, 2018	Jubert, 2017	Finogejevs, 2020	Khan, 2018	Nabj, B. N. 2018	Phul, 2018	Huang, 2019
<p>↑ Better Outcomes</p> <p>↓ Worse Outcomes</p> <p>● Not Significant</p>								
Composite								
WOMAC Total		↑						↑
Function								
IKDC				↑				
WOMAC Function		↑			●			
WOMAC Stiffness		↓			●			
KOOS Symptoms	↑		●					
KOOS ADL	↑		●					
KOOS Sports/Rec	●		●					
Lequesne Index		↑						
SF-36 Physical Component Summary			●					
20 min walk test (sec)	↓							
SF-36 Physical Function			●					
SF-36 Physical Role Function			●					
Knee Society Score				↑				

Pain/QOL

	High						Moderate
	Forogh, 2016	Guvendi, 2018	Jubert, 2017	Finogejevs, 2020	Khan, 2018	Nabi, B. N. 2018	Phul, 2018 Huang, 2019
Pain							
VAS Pain score	↑	↑	●	↑	↓	●	↑ ●
WOMAC Pain		↑			●		
KOOS Pain	↑		●				
SF-36 Bodily Pain			●				
Visual Numeric Scale scores- Time		↑					
VAS Pain During Walking		↑					
QOL							
KOOS QOL	↑		●				
SF-36 Vitality			●				
SF-36 Mental Component Summary			●				
SF-36 General Health perception			●				
SF-36 Social Functioning			●				
SF-36 Emotional Role Function			●				
SF-36 Mental Health			●				

Adverse Events

	High						Moderate
	Forogh, 2016	Guvendi, 2018	Jubert, 2017	Finogejevs, 2020	Khan, 2018	Nabi, B. N. 2018	Phul, 2018
<p> ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant </p>							
Adverse Events							
Infection							●
Low-Grade Fever							●●
Pain							●●
Deep Vein Thrombosis							●

SOF: PRP vs. Exercise

	High					Moderate
	Rayegani, 2014	Elgendy, 2020	Raessadat, S. A. 2020	Akan, Ö 2018	Gaballa, 2019	
<p> ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant </p>						
Composite						
WOMAC Total		↑				
Function						
WOMAC Function	●			●	↑	
WOMAC Stiffness	●		●	●		
Knee Flexion ROM		↓				
6 min walk					↑	
Other						
Functional capacity			●			
Pain						
VAS Pain score		↑			↑	
WOMAC Pain	●		●	↑		

SOF: PRP vs. Prolotherapy

	High	Moderate
	Rahimzadeh, 2018	Eroglu, 2016
<p> ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant </p>		
Composite		
WOMAC Total	↑	●
Function		
WOMAC Function	↑	●
WOMAC Stiffness	↑	●
Pain		
WOMAC Pain	↑	●

SOF: PRP vs. ACS

	Moderate
<ul style="list-style-type: none"> ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant 	Pishgahi, A.2020
Composite	
WOMAC Total	↓
Pain	
VAS Pain score	↓

SOF: PRP vs. BMAC

	Moderate
<ul style="list-style-type: none"> ↑ Better Outcomes ↓ Worse Outcomes ● Not Significant 	Anz, 2020
Composite	
WOMAC Total	●
Function	
IKDC	●
WOMAC Function	●
WOMAC Stiffness	●
Pain	
WOMAC Pain	↑

SOF: PRP vs. HA

Composite

	High														Moderate												
	Cole, 2017	Raeissadat, 2015	Lin, 2019	Ahmad, 2018	Lisi, 2018	Tavassoli, 2019	Heredia, 2016	Raeissadat, 2020	Di Martino, 2019	Buendia-Lopez, 2018	Sanchez, 2012	Vaquerizo, 2013	Gormeli, 2017	Louis, M. L. 2018	Park, 2021	Xu, 2021	Raeissadat, 2021	Bansal, 2021	Huang, 2019	Raeissadat, 2017	Lana, 2016	Spakova, 2012	Cerza, 2012	Duymus, 2017	Basnaev, 2021	Su, K. 2018	
Composite																											
WOMAC Total		↑	↑		●	↑		↑		↑	●	↑		●	↑		↑	↑	↑	●		↑	↑	↑		↑	
Lequesne Index					●																						
LEQ Total								↑									↑			●							
WOMAC Total (30% decrease)						↑		↑																			
WOMAC Total (50% decrease)						↑																					
Lysholm Scale Score					●																						

Function

	High										Moderate															
	Cole, 2017	Raeisadat, 2015	Lin, 2019	Ahmad, 2018	Lisi, 2018	Tavassoli, 2019	Heredia, 2016	Raeisadat, 2020	Di Martino, 2019	Buendia-Lopez, 2018	Sanchez, 2012	Vaquerizo, 2013	Gormeli, 2017	Louis, M. L. 2018	Park, 2021	Xu, 2021	Raeisadat, 2021	Bansal, 2021	Huang, 2019	Raeisadat, 2017	Lana, 2016	Spakova, 2012	Cerza, 2012	Duyumus, 2017	Baanaev, 2021	Su, K. 2018
Function																										
IKDC	↑		↑	↑											↑											
WOMAC Function	↑	↑																								
WOMAC Stiffness	↑				●	↑		↑		↑	●	↑		●	↑					●	●			↑	↑	↑
KOOS ADL																										
KOOS Sports/Rec																										
Lequesne Index																										
SF-36 Physical Component																										
Summary		↑																								
KOOS Scores																										
EQ Mobility																										
EQ Daily Activity																										
LEQ Walking																										
LEQ ADL																										
IKDC; Early OA																										
Functional Scores																										
SF-36 Physical Function		↑																								
SF-36 Physical Role Function		↑																								
PCS-36 and MCS?36		●																								
WOMAC Stiffness (30% decrease)																										
WOMAC Function (30% decrease)																										
WOMAC Stiffness (50% decrease)																										
WOMAC Function (50% decrease)																										
WOMAC Function, 20% Decrease																										
WOMAC Stiffness, 20% Decrease																										
IKDC; Advanced OA																										
SMC Patellofemoral Function																										
Pain Free Distance During 6MWT																										
WOMAC ADL																										
AKSS																										
Tegner Scale																										

Pain

	High										Moderate															
	Cole, 2017	Raeissadat, 2015	Lin, 2019	Ahmad, 2018	Lisi, 2018	Tavassoli, 2019	Heredia, 2016	Raeissadat, 2020	Di Martino, 2019	Buendia-Lopez, 2018	Sanchez, 2012	Vaquerizo, 2013	Gormeli, 2017	Louis, M. L. 2018	Park, 2021	Xu, 2021	Raeissadat, 2021	Bansal, 2021	Huang, 2019	Raeissadat, 2017	Lana, 2016	Spakova, 2012	Cerza, 2012	Duymus, 2017	Basnaev, 2021	Su, K. 2018
Pain																										
VAS Pain score	↑			↑	●	↑		↑		↑			●	↓			↑	↑	●	●	↑	↑		↑	↓	↑
WOMAC Pain	●	●			●	↑		●		↑	●	↑		●	●		↑	↑		●	●			↑	↓	↑
KOOS Pain							↑																			
SF-36 Bodily Pain		↑																								
LEQ Pain								↓									↓		●							
EQ Pain							●					↑														
EUROQOL Pain																										
Scale-Improvement							●																			
VAS Pain During Walking																									↓	
WOMAC Pain (30% decrease)						↑		●																		
WOMAC Pain (50% decrease)						↑																				
VAS Pain score (50% decrease)					↑		●																			
EUROQOL Pain																										
Scale- Worsening							●																			
EUROQOL Pain Scale- Similar							●																			
WOMAC Pain, 20% Decrease										↑	●															
WOMAC Pain, 50% Decrease										↑																
EQ-VAS; Early OA													↑													
EQ-VAS; Advanced OA													●													
SMC																										
Patellofemoral Pain															●											

QOL

	High															Moderate											
	Cole, 2017	Raeissadat, 2015	Lin, 2019	Ahmad, 2018	Lisi, 2018	Tavassoli, 2019	Heredia, 2016	Raeissadat, 2020	Di Martino, 2019	Buendia-Lopez, 2018	Sanchez, 2012	Vaquerizo, 2013	Gormeli, 2017	Louis, M. L. 2018	Park, 2021	Xu, 2021	Raeissadat, 2021	Bansal, 2021	Huang, 2019	Raeissadat, 2017	Lana, 2016	Spakova, 2012	Cerza, 2012	Duymus, 2017	Basnaev, 2021	Su, K. 2018	
QOL																											
SF-36 Vitality		●																									
SF-36 Mental Component Summary		↑																									
EQ Personal Care							●																				
EQ (VAS)								↑																			
SF-36 General Health perception		↑																									
SF-36 Social Functioning		↑																									
SF-36 Emotional Role Function		●																									
SF-36 Mental Health		↑																									
Lequesne scale scores- walk																					●						
Lequesne scale scores- daily life																					●						

↑ Better Outcomes
 ↓ Worse Outcomes
 ● Not Significant

Adverse Events

	High											Moderate															
	Cole, 2017	Raeissadat, 2015	Lin, 2019	Ahmad, 2018	Lisi, 2018	Tavassoli, 2019	Heredia, 2016	Raeissadat, 2020	Di Martino, 2019	Buendia-Lopez, 2018	Sanchez, 2012	Vaquerizo, 2013	Gormeli, 2017	Louis, M. L. 2018	Park, 2021	Xu, 2021	Raeissadat, 2021	Bansal, 2021	Huang, 2019	Raeissadat, 2017	Lana, 2016	Spakova, 2012	Cerza, 2012	Duymus, 2017	Basnaev, 2021	Su, K. 2018	
Adverse Events																											
Infection																				●							
Low-Grade Fever																				●							
Pain																				●							
Effusion				↑																●							
Any AE												●															
Injection Site Pain															●												
Joint Swelling																●											
Deep Vein Thrombosis																				●							
Minor complications due to injection																				●							
Injection-induced pain score																											
Synovial vascularity				↑																							
Synovial hypertrophy				↑																							
Minor complication due to injection																											
System Organ Class AE																											
Injection Site Swelling															●												
Pain after Injection															●												

↑ Better Outcomes
 ↓ Worse Outcomes
 ● Not Significant

SOF: PRP vs. Ozone Therapy

	High		Moderate	
	Raeissadat, 2021	Gaballa, 2019	Duymus, 2017	
<p>↑ Better Outcomes</p> <p>↓ Worse Outcomes</p> <p>● Not Significant</p>				
Composite				
WOMAC Total	↑			↑
LEQ Total	↑			
Function				
WOMAC Function	↑	↑		↑
WOMAC Stiffness	↑			↑
6 min walk		↑		
LEQ Walking	↑			
LEQ ADL	↑			
Pain				
VAS Pain score	↑	↑		↑
WOMAC Pain	↑			↑
LEQ Pain	↑			

Data Tables

Table 1: PICO 1a- 1: Platelet rich plasma vs. 1: Acetaminophen- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Simental-Mendia,2016	Moderate	WOMAC Total	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	WOMAC Total	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	WOMAC Total	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen

Table 2: PICO 1a- 1: Platelet rich plasma vs. 1: Acetaminophen- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Simental-Mendia,2016	Moderate	VAS Functional Capacity	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Functional Capacity	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Functional Capacity	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Stiffness	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Stiffness	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Stiffness	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen

Table 3: PICO 1a- 1: Platelet rich plasma vs. 1: Acetaminophen- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Simental-Mendia,2016	Moderate	VAS Pain score	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Pain score	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Mean Difference	-2.2 (-3.25, -1.15)	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	VAS Pain score	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen

Table 4: PICO 1a- 1: Platelet rich plasma vs. 1: Acetaminophen- QOL

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Simental-Mendia,2016	Moderate	SF Mean Physical Component	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	SF Mean Physical Component	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	SF Mean Physical Component	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	SF Mean Mental Component	6 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	SF Mean Mental Component	12 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	SF Mean Mental Component	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen
Simental-Mendia,2016	Moderate	QOL Score	24 wks	Leukocyte-Poor Platelet Rich Plasma: One Injection every two weeks for six weeks	Acetaminophen: acetaminophen (500 mg/8 h) over 6 weeks	Author Reported - Chi-Squared and Fisher's Exact Test	N/A	Leukocyte-Poor Platelet-Rich Plasma favored over Acetaminophen

Table 5: PICO 1b- 1: Platelet rich plasma vs. 1: ACS- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Pishgahi, A.2020	Moderate	WOMAC Total (WOMAC Scores)	1 mos	PRP treatment	Autologous Conditioned Serum: Combo of centrifuged blood and bioactive materials	Mean Difference	-3.06 (-5.06, -1.06)	PRP treatment
Pishgahi, A.2020	Moderate	WOMAC Total (WOMAC Scores)	6 mos	PRP treatment	Autologous Conditioned Serum: Combo of centrifuged blood and bioactive materials	Mean Difference	10.79 (9.00, 12.58)	Autologous Conditioned Serum

Table 6: PICO 1b- 1: Platelet rich plasma vs. 1: ACS- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Pishgahi, A.2020	Moderate	VAS Pain score (VAS)	1 mos	PRP treatment	Autologous Conditioned Serum: Combo of centrifuged blood and bioactive materials	Mean Difference	9.45 (7.87, 11.03)	Autologous Conditioned Serum
Pishgahi, A.2020	Moderate	VAS Pain score (VAS)	6 mos	PRP treatment	Autologous Conditioned Serum: Combo of centrifuged blood and bioactive materials	Mean Difference	20 (18.54, 21.46)	Autologous Conditioned Serum

Table 7: PICO 1c- 1: Platelet rich plasma vs. 1: bone marrow aspirate concentrate (BMC)- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Anz, 2020	Moderate	WOMAC Total	1 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.3 (-6.91, 6.31)	NS
Anz, 2020	Moderate	WOMAC Total	3 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	3 (-3.18, 9.18)	NS
Anz, 2020	Moderate	WOMAC Total	6 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-3.2 (-10.11, 3.71)	NS
Anz, 2020	Moderate	WOMAC Total	9 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0.8 (-6.34, 7.94)	NS
Anz, 2020	Moderate	WOMAC Total	12 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-2.6 (-9.71, 4.51)	NS

Table 8: PICO 1c- 1: Platelet rich plasma vs. 1: bone marrow aspirate concentrate (BMC)- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Anz, 2020	Moderate	IKDC	1 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.1 (-8.15, 7.95)	NS
Anz, 2020	Moderate	WOMAC Function	1 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.2 (-4.79, 4.39)	NS
Anz, 2020	Moderate	WOMAC Stiffness	1 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0 (-0.62, 0.62)	NS
Anz, 2020	Moderate	IKDC	3 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-2 (-9.35, 5.35)	NS
Anz, 2020	Moderate	WOMAC Function	3 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	2.7 (-1.79, 7.19)	NS
Anz, 2020	Moderate	WOMAC Stiffness	3 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0.1 (-0.52, 0.72)	NS
Anz, 2020	Moderate	IKDC	6 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	1.3 (-7.36, 9.96)	NS
Anz, 2020	Moderate	WOMAC Function	6 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-1.3 (-6.07, 3.47)	NS
Anz, 2020	Moderate	WOMAC Stiffness	6 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.2 (-0.86, 0.46)	NS
Anz, 2020	Moderate	IKDC	9 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.6 (-9.60, 8.40)	NS
Anz, 2020	Moderate	WOMAC Function	9 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0.9 (-4.12, 5.92)	NS
Anz, 2020	Moderate	WOMAC Stiffness	9 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.3 (-0.99, 0.39)	NS
Anz, 2020	Moderate	IKDC	12 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.6 (-9.25, 8.05)	NS
Anz, 2020	Moderate	WOMAC Function	12 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-1.5 (-6.61, 3.61)	NS
Anz, 2020	Moderate	WOMAC Stiffness	12 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.5 (-1.16, 0.16)	NS

Table 9: PICO 1c- 1: Platelet rich plasma vs. 1: bone marrow aspirate concentrate (BMC)- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Anz, 2020	Moderate	WOMAC Pain	1 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.1 (-1.54, 1.34)	NS
Anz, 2020	Moderate	WOMAC Pain	3 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0.3 (-1.03, 1.63)	NS
Anz, 2020	Moderate	WOMAC Pain	6 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-1.5 (-2.94, -0.06)	PRP treatment
Anz, 2020	Moderate	WOMAC Pain	9 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	0.3 (-1.16, 1.76)	NS
Anz, 2020	Moderate	WOMAC Pain	12 mos	PRP treatment: single 7ml inj.	Bone-marrow Aspirate Concentrate: single 7ml inj.	Mean Difference	-0.6 (-1.93, 0.73)	NS

Table 10: PICO 1d- 1: Platelet rich plasma vs. 1: Corticosteroid- Adverse Events

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Huang, 2019	Moderate	Deep Vein Thrombosis	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Infection	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Low-Grade Fever	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Pain	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	RR	1.67(0.43,6.51)	NS

Table 11: PICO 1d- 1: Platelet rich plasma vs. 1: Corticosteroid- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Guvendi, 2018	High	WOMAC Total	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-7.3 (-10.42, -4.18)	PRP treatment
Guvendi, 2018	High	WOMAC Total	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-16.1 (-19.61, -12.59)	PRP treatment
Guvendi, 2018	High	WOMAC Total	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-7.1 (-11.17, -3.03)	PRP treatment
Guvendi, 2018	High	WOMAC Total	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	0 (-3.96, 3.96)	NS
Huang, 2019	Moderate	WOMAC Total	3 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	Mean Difference	0.37 (-1.78, 2.52)	NS
Huang, 2019	Moderate	WOMAC Total	6 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	Mean Difference	-3.86 (-6.01, -1.71)	
Huang, 2019	Moderate	WOMAC Total	9 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	Mean Difference	-8.04 (-10.19, -5.89)	
Huang, 2019	Moderate	WOMAC Total	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	Mean Difference	-16.08 (-19.17, -12.99)	

Table 12: PICO 1d- 1: Platelet rich plasma vs. 1: Corticosteroid- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Forogh, 2016	High	KOOS Symptoms	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	14.7 (4.23, 25.17)	PRP treatment
Forogh, 2016	High	KOOS ADL	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	20.3 (9.00, 31.60)	PRP treatment
Forogh, 2016	High	KOOS Sports/Rec	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	2.7 (-2.54, 7.94)	NS
Forogh, 2016	High	KOOS Symptoms	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	19.8 (11.12, 28.48)	PRP treatment
Forogh, 2016	High	KOOS ADL	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	12 (0.81, 23.19)	PRP treatment
Forogh, 2016	High	KOOS Sports/Rec	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	-0.3 (-6.35, 5.75)	NS
Forogh, 2016	High	20 min walk test (sec)	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	-3.3 (-6.05, -0.55)	Corticosteroid treatment
Forogh, 2016	High	20 min walk test (sec)	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	-2.6 (-5.63, 0.43)	NS
Guvendi, 2018	High	Lequesne Index	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-0.9 (-1.73, -0.07)	PRP treatment
Guvendi, 2018	High	Lequesne Index	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-2.9 (-3.72, -2.08)	PRP treatment
Guvendi, 2018	High	WOMAC Function	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-5.5 (-7.79, -3.21)	PRP treatment
Guvendi, 2018	High	WOMAC Stiffness	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-0.3 (-0.63, 0.03)	NS
Guvendi, 2018	High	WOMAC Function	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-9.9 (-12.36, -7.44)	PRP treatment
Guvendi, 2018	High	WOMAC Stiffness	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.7 (-2.10, -1.30)	PRP treatment
Guvendi, 2018	High	Lequesne Index	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.4 (-2.25, -0.55)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Guvendi, 2018	High	Lequesne Index	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-3.1 (-3.96, -2.24)	PRP treatment
Guvendi, 2018	High	WOMAC Function	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-4.3 (-7.42, -1.18)	PRP treatment
Guvendi, 2018	High	WOMAC Stiffness	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	0.5 (0.11, 0.89)	Corticosteroid treatment
Guvendi, 2018	High	WOMAC Function	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-13.1 (-15.91, -10.29)	PRP treatment
Guvendi, 2018	High	WOMAC Stiffness	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.9 (-2.40, -1.40)	PRP treatment
Jubert, 2017	High	KOOS Symptoms	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-2 (-8.33, 4.33)	NS
Jubert, 2017	High	KOOS ADL	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-3.04 (-14.20, 8.12)	NS
Jubert, 2017	High	KOOS Sports/Rec	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-10.86 (-22.26, 0.54)	NS
Jubert, 2017	High	KOOS Symptoms	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-1.81 (-9.05, 5.43)	NS
Jubert, 2017	High	KOOS ADL	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	2.89 (-8.42, 14.20)	NS
Jubert, 2017	High	KOOS Sports/Rec	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.47 (-12.15, 11.21)	NS
Jubert, 2017	High	KOOS Symptoms	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-3.94 (-10.04, 2.16)	NS
Jubert, 2017	High	KOOS ADL	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	9.39 (-2.13, 20.91)	NS
Jubert, 2017	High	KOOS Sports/Rec	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	2.86 (-8.52, 14.24)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Jubert, 2017	High	SF-36 Physical Function (physical health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.87 (-10.77, 12.51)	NS
Jubert, 2017	High	SF-36 Physical Role Function (physical health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.65 (-4.27, 5.57)	NS
Jubert, 2017	High	SF-36 Physical Component Summary (physical health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.01 (-0.31, 0.29)	NS
Jubert, 2017	High	SF-36 Physical Function (physical health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	3.34 (-7.73, 14.41)	NS
Jubert, 2017	High	SF-36 Physical Role Function (physical health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.15 (-5.29, 5.59)	NS
Jubert, 2017	High	SF-36 Physical Component Summary (physical health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.11 (-0.41, 0.19)	NS
Jubert, 2017	High	SF-36 Physical Function (physical health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	7.1 (-3.56, 17.76)	NS
Jubert, 2017	High	SF-36 Physical Role Function (physical health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.21 (-4.34, 4.76)	NS
Jubert, 2017	High	SF-36 Physical Component Summary (physical health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.09 (-0.18, 0.36)	NS
Finogejevs, 2020	High	IKDC (V1)	0 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	7.4 (1.18, 13.62)	PRP treatment
Finogejevs, 2020	High	IKDC (V2)	1 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-4.7 (-13.78, 4.38)	NS
Finogejevs, 2020	High	IKDC (V3)	5 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	4.7 (-5.92, 15.32)	NS
Finogejevs, 2020	High	IKDC (V4)	15 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	20.5 (11.37, 29.63)	PRP treatment
Finogejevs, 2020	High	IKDC (V5)	30 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	21.2 (10.75, 31.65)	PRP treatment
Finogejevs, 2020	High	IKDC (V6)	58 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	22.2 (11.75, 32.65)	PRP treatment
Finogejevs, 2020	High	Knee Society Score (V1)	0 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	4.6 (-0.51, 9.71)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Finogejevs, 2020	High	Knee Society Score (V2)	1 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-1.9 (-9.27, 5.47)	NS
Finogejevs, 2020	High	Knee Society Score (V3)	5 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	4.8 (-2.25, 11.85)	NS
Finogejevs, 2020	High	Knee Society Score (V4)	15 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	15.6 (7.96, 23.24)	PRP treatment
Finogejevs, 2020	High	Knee Society Score (V5)	30 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	15.6 (7.17, 24.03)	PRP treatment
Finogejevs, 2020	High	Knee Society Score (V6)	58 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	17 (8.54, 25.46)	PRP treatment
Khan, 2018	High	WOMAC Stiffness	6 mos	PRP treatment: 5ml platelet rich plasma injection	Corticosteroid treatment: one ml (40mg) of triamcinolone acetonide and 4 ml of 1% lidocaine hydrochloride mix in 10 ml syringe	Mean Difference	0.28 (-0.32, 0.88)	NS
Khan, 2018	High	WOMAC Function	6 mos	PRP treatment: 5ml platelet rich plasma injection	Corticosteroid treatment: one ml (40mg) of triamcinolone acetonide and 4 ml of 1% lidocaine hydrochloride mix in 10 ml syringe	Mean Difference	1.64 (-0.89, 4.17)	NS

Table 13: PICO 1d- 1: Platelet rich plasma vs. 1: Corticosteroid- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Forogh, 2016	High	KOOS Pain	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	13.5 (3.43, 23.57)	PRP treatment
Forogh, 2016	High	KOOS Pain	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	23.6 (12.72, 34.48)	PRP treatment
Forogh, 2016	High	VAS Pain score	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	-20.2 (-33.65, -6.75)	PRP treatment
Forogh, 2016	High	VAS Pain score	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	-27.9 (-38.08, -17.72)	PRP treatment
Guvendi, 2018	High	VAS Pain score	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-0.8 (-1.23, -0.37)	PRP treatment
Guvendi, 2018	High	Visual Numeric Scale scores-Time	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	0 (-0.39, 0.39)	NS
Guvendi, 2018	High	VAS Pain During Walking	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.7 (-2.19, -1.21)	PRP treatment
Guvendi, 2018	High	VAS Pain score	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.9 (-2.39, -1.41)	PRP treatment
Guvendi, 2018	High	Visual Numeric Scale scores-Time	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.7 (-2.26, -1.14)	PRP treatment
Guvendi, 2018	High	VAS Pain During Walking	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-2.6 (-3.16, -2.04)	PRP treatment
Guvendi, 2018	High	WOMAC Pain	2 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.6 (-2.32, -0.88)	PRP treatment
Guvendi, 2018	High	WOMAC Pain	6 mos	PRP treatment: Single PRP inj.	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-4.8 (-5.67, -3.93)	PRP treatment
Guvendi, 2018	High	VAS Pain score	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.8 (-2.14, -1.46)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Guvendi, 2018	High	Visual Numeric Scale scores-Time	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-1.3 (-1.63, -0.97)	PRP treatment
Guvendi, 2018	High	VAS Pain During Walking	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-3.3 (-3.76, -2.84)	PRP treatment
Guvendi, 2018	High	VAS Pain score	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-2.2 (-2.77, -1.63)	PRP treatment
Guvendi, 2018	High	Visual Numeric Scale scores-Time	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-2.2 (-2.80, -1.60)	PRP treatment
Guvendi, 2018	High	VAS Pain During Walking	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-3.2 (-3.84, -2.56)	PRP treatment
Guvendi, 2018	High	WOMAC Pain	2 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-3.5 (-4.25, -2.75)	PRP treatment
Guvendi, 2018	High	WOMAC Pain	6 mos	PRP treatment: 3 inj. of PRP	Corticosteroid treatment: 1 inj. of 1mL suspension containing 6.43 mg of betamethasone dipropionate and 2.63 mg of betamethasone sodium phosphate	Mean Difference	-4.9 (-5.96, -3.84)	PRP treatment
Jubert, 2017	High	VAS Pain score	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	4.21 (-7.25, 15.67)	NS
Jubert, 2017	High	VAS Pain score	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-7.62 (-19.89, 4.65)	NS
Jubert, 2017	High	VAS Pain score	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-8.09 (-21.65, 5.47)	NS
Jubert, 2017	High	KOOS Pain	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-5.93 (-17.44, 5.58)	NS
Jubert, 2017	High	KOOS Pain	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.49 (-10.48, 11.46)	NS
Jubert, 2017	High	KOOS Pain	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	3.57 (-7.72, 14.86)	NS
Jubert, 2017	High	SF-36 Bodily Pain (physical health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-3.9 (-15.94, 8.14)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Jubert, 2017	High	SF-36 Bodily Pain (physical health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.64 (-11.30, 12.58)	NS
Jubert, 2017	High	SF-36 Bodily Pain (physical health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	4 (-6.72, 14.72)	NS
Finogeevs, 2020	High	VAS Pain score (V1)	0 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-53.9 (-54.82, -52.98)	PRP treatment
Finogeevs, 2020	High	VAS Pain score (V2)	1 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	0.7 (-0.54, 1.94)	NS
Finogeevs, 2020	High	VAS Pain score (V3)	5 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-0.2 (-1.28, 0.88)	NS
Finogeevs, 2020	High	VAS Pain score (V4)	15 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-2.2 (-3.33, -1.07)	PRP treatment
Finogeevs, 2020	High	VAS Pain score (V5)	30 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-2.4 (-3.54, -1.26)	PRP treatment
Finogeevs, 2020	High	VAS Pain score (V6)	58 wks	PRP treatment: 8 mL of an intraarticular infiltration of PRP (single inj.)	Corticosteroid treatment: 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) (single inj.)	Mean Difference	-2.2 (-3.33, -1.07)	PRP treatment
Phul, 2018	Moderate	VAS Pain score	3 mos	PRP treatment: 4–6 mL of platelet rich plasma with concentration of 4–5 times standard usual values; contained Leukocytes; Two hours before injection, a single dose of acetaminophen-codeine was given	Corticosteroid treatment: 40 mg triamcinolone hexacetonide+ 10 mg bupivacaine	Mean Difference	-0.9 (-1.26, -0.54)	PRP treatment
Khan, 2018	High	VAS Pain score	6 mos	PRP treatment: 5ml platelet rich plasma injection	Corticosteroid treatment: one ml (40mg) of triamcinolone acetonide and 4 ml of 1% lidocaine hydrochloride mix in 10 ml syringe	Mean Difference	0.485 (0.03, 0.94)	Corticosteroid treatment
Khan, 2018	High	WOMAC Pain	6 mos	PRP treatment: 5ml platelet rich plasma injection	Corticosteroid treatment: one ml (40mg) of triamcinolone acetonide and 4 ml of 1% lidocaine hydrochloride mix in 10 ml syringe	Mean Difference	-1.08 (-2.32, 0.16)	NS
Huang, 2019	Moderate	VAS Pain score	12 mos	4 ml three times every three weeks	Corticosteroid treatment: 1 ml three times every three weeks	Mean Difference	-0.28 (-0.97, 0.41)	NS
Nabi, B. N. 2018	High	VAS Pain score	0 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	-0.24 (-10.48, 10.00)	NS
Nabi, B. N. 2018	High	VAS Pain score	1 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.52 (-6.79, 7.83)	NS
Nabi, B. N. 2018	High	VAS Pain score	2 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.66 (-5.57, 6.89)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Nabi, B. N. 2018	High	VAS Pain score	3 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.55 (-5.07, 6.17)	NS
Nabi, B. N. 2018	High	VAS Pain score	4 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	1.36 (-4.56, 7.28)	NS
Nabi, B. N. 2018	High	VAS Pain score	0 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	-0.24 (-10.48, 10.00)	NS
Nabi, B. N. 2018	High	VAS Pain score	1 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.52 (-6.79, 7.83)	NS
Nabi, B. N. 2018	High	VAS Pain score	2 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.66 (-5.57, 6.89)	NS
Nabi, B. N. 2018	High	VAS Pain score	3 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	0.55 (-5.07, 6.17)	NS
Nabi, B. N. 2018	High	VAS Pain score	4 mos	PRP treatment: PRP intra-articular injection (group P)	Corticosteroid treatment: intra-articular injection of Triamcinolone (group T).	Mean Difference	1.36 (-4.56, 7.28)	NS

Table 14: PICO 1d- 1: Platelet rich plasma vs. 1: Corticosteroid- QOL

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Forogh, 2016	High	KOOS QOL	2 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	7.8 (-2.18, 17.78)	NS
Forogh, 2016	High	KOOS QOL	6 mos	PRP treatment: 5ml of PRP + activated by 0.5ml of calcium gluconate solution	Corticosteroid treatment: 1 ml of Depo-Medrol (40mg of methylprednisolone acetate)	Mean Difference	13.1 (4.84, 21.36)	PRP treatment
Jubert, 2017	High	KOOS QoL	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-4.04 (-13.86, 5.78)	NS
Jubert, 2017	High	KOOS QoL	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	9.17 (-1.04, 19.38)	NS
Jubert, 2017	High	KOOS QoL	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	10.04 (-1.53, 21.61)	NS
Jubert, 2017	High	SF-36 General Health perception (physical health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-7.06 (-14.86, 0.74)	NS
Jubert, 2017	High	SF-36 Vitality (mental health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-3.52 (-15.07, 8.03)	NS
Jubert, 2017	High	SF-36 Social Functioning (mental health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.05 (-14.75, 14.85)	NS
Jubert, 2017	High	SF-36 Emotional Role Function (mental health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.77 (-5.20, 6.74)	NS
Jubert, 2017	High	SF-36 Mental Health (mental health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-4.22 (-15.19, 6.75)	NS
Jubert, 2017	High	SF-36 Mental Component Summary (mental health dimension)	1 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.08 (-0.49, 0.33)	NS
Jubert, 2017	High	SF-36 General Health perception (physical health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-6.67 (-15.16, 1.82)	NS
Jubert, 2017	High	SF-36 Vitality (mental health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.75 (-10.51, 12.01)	NS
Jubert, 2017	High	SF-36 Social Functioning (mental health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-2.06 (-17.08, 12.96)	NS
Jubert, 2017	High	SF-36 Emotional Role Function (mental health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-1.19 (-7.15, 4.77)	NS
Jubert, 2017	High	SF-36 Mental Health (mental health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.45 (-11.67, 10.77)	NS
Jubert, 2017	High	SF-36 Mental Component Summary (mental health dimension)	3 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.11 (-0.54, 0.32)	NS
Jubert, 2017	High	SF-36 General Health perception (physical health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	-0.06 (-9.13, 9.01)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Jubert, 2017	High	SF-36 Vitality (mental health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	4.37 (-7.15, 15.89)	NS
Jubert, 2017	High	SF-36 Social Functioning (mental health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	3.79 (-12.66, 20.24)	NS
Jubert, 2017	High	SF-36 Emotional Role Function (mental health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.09 (-5.89, 6.07)	NS
Jubert, 2017	High	SF-36 Mental Health (mental health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	6.6 (-1.21, 14.41)	NS
Jubert, 2017	High	SF-36 Mental Component Summary (mental health dimension)	6 mos	Leukocyte-Poor Platelet Rich Plasma: leukocyte reduced PRP; single inj. Of 4 mL autologous PRP	Corticosteroid treatment: 6 mg betamethasone sodium phosphate	Mean Difference	0.23 (-0.23, 0.69)	NS

Table 15: PICO 1d- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Cole, 2017	High	WOMAC Pain	6 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Mean Difference	-0.09 (-6.62, 6.44)	NS
Cole, 2017	High	WOMAC Pain	12 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Mean Difference	-1.02 (-7.41, 5.37)	NS
Cole, 2017	High	WOMAC Pain	24 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Mean Difference	-0.89 (-7.36, 5.58)	NS
Cole, 2017	High	WOMAC Pain	52 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Mean Difference	-0.98 (-5.99, 4.03)	NS

Table 16: PICO 1e- 1: Platelet rich plasma vs. 1: Exercise/PT- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rayegani, 2014	High	SF-36	Postop.	Leukocyte-PRP treatment + therapeutic exercise: two courses of leukocyte rich PRP (5.6 fold higher platelet concentration) with a4-week interval + therapeutic exercise same as control group	therapeutic exercise: multiangle isometric exercises, stretching. And after4 weeks, concentric exercises of the quadriceps, adductors and abductors were taught to the patient.	Author Reported - not given	N/A	PRP Treatment
Elgendy, 2020	High	WOMAC Total	4 wks	PRP injection: Single injection 6mL	Standard PT: 1 session/wk for 4 wks	Mean Difference	-36.34 (-38.77, -33.91)	PRP injection

Table 17: PICO 1e- 1: Platelet rich plasma vs. 1: Exercise/PT- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rayegani, 2014	High	WOMAC Stiffness	6 mos	Leukocyte-PRP treatment + therapeutic exercise: two courses of leukocyte rich PRP (5.6 fold higher platelet concentration) with a4-week interval + therapeutic exercise same as control group	therapeutic exercise: multiangle isometric exercises, stretching. And after4 weeks, concentric exercises of the quadriceps, adductors and abductors were taught to the patient.	Mean Difference	0 (-0.64, 0.64)	NS
Rayegani, 2014	High	WOMAC Function	6 mos	Leukocyte-PRP treatment + therapeutic exercise: two courses of leukocyte rich PRP (5.6 fold higher platelet concentration) with a4-week interval + therapeutic exercise same as control group	therapeutic exercise: multiangle isometric exercises, stretching. And after4 weeks, concentric exercises of the quadriceps, adductors and abductors were taught to the patient.	Mean Difference	0.17 (-5.54, 5.88)	NS
Elgendy, 2020	High	Knee Flexion ROM	4 wks	PRP injection: Single injection 6mL	Standard PT: 1 session/wk for 4 wks	Mean Difference	17.8 (13.56, 22.04)	Standard PT
Raeissadat, S. A.2020	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	8 mos	PRP treatment	Exercise	Mean Difference	-0.24 (-0.82, 0.34)	NS
Akan, Ö 2018	High	WOMAC stiffness (Median)	3 mos	PRP+EXERCISE	Exercise	Mean Difference	0.5 (-4.46, 5.46)	NS
Akan, Ö 2018	High	WOMAC stiffness (Median)	6 mos	PRP+EXERCISE	Exercise	Mean Difference	2.5 (-3.09, 8.09)	NS
Akan, Ö 2018	High	WOMAC Function (Median)	3 mos	PRP+EXERCISE	Exercise	Mean Difference	1.185 (-6.14, 8.51)	NS
Akan, Ö 2018	High	WOMAC Function (Median)	6 mos	PRP+EXERCISE	Exercise	Mean Difference	3.605 (-4.15, 11.36)	NS
Gaballa, 2019	Moderate	WOMAC Function	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS)	Mean Difference	-24.4 (-28.81, -19.99)	PRP treatment
Gaballa, 2019	Moderate	WOMAC Function	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS)	Mean Difference	-29.3 (-34.60, -24.00)	PRP treatment
Gaballa, 2019	Moderate	6 min walk	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS)	Mean Difference	-3.3 (-35.66, 29.06)	NS
Gaballa, 2019	Moderate	6 min walk	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS)	Mean Difference	43.3 (6.09, 80.51)	PRP treatment

Table 18: PICO 1e- 1: Platelet rich plasma vs. 1: Exercise/PT- Other

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, S. A.2020	High	Functional capacity (WOMAC Osteoarthritis Index Scores)	8 mos	PRP treatment	Exercise	Mean Difference	-1.9 (-6.26, 2.46)	NS

Table 19: PICO 1e- 1: Platelet rich plasma vs. 1: Exercise/PT- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rayegani, 2014	High	WOMAC Pain	6 mos	Leukocyte-PRP treatment + therapeutic exercise: two courses of leukocyte rich PRP (5.6 fold higher platelet concentration) with a 4-week interval + therapeutic exercise same as control group	therapeutic exercise: multiangle isometric exercises of muscles around the knee (quadriceps muscle, adductors and abductors of the thigh) as well as stretching of the hamstring 3 times a day and every move lasting 10 seconds and repeated 10 times. And after 4 weeks, concentric exercises of the quadriceps, adductors and abductors were taught to the patient.	Mean Difference	-0.96 (-2.88, 0.96)	NS
Elgendy, 2020	High	VAS Pain score	4 wks	PRP injection: Single injection 6mL	Standard PT: 1 session/wk for 4 wks	Mean Difference	-2.99 (-3.45, -2.53)	PRP injection
Raeissadat, S. A.2020	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	8 mos	PRP treatment	Exercise	Mean Difference	-0.19 (-1.90, 1.52)	NS
Raeissadat, S. A.2020	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	8 mos	PRP treatment	Exercise	Mean Difference	-0.66 (-1.79, 0.47)	NS
Akan, Ö 2018	High	WOMAC pain	3 mos	PRP+EXERCISE	Exercise	Mean Difference	1.816 (0.59, 3.04)	PRP+EXERCISE
Akan, Ö 2018	High	WOMAC pain	6 mos	PRP+EXERCISE	Exercise	Mean Difference	2.7 (1.38, 4.02)	PRP+EXERCISE
Gaballa, 2019	Moderate	VAS Pain score	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS), quadriceps muscle strengthening exercises (quadriceps setting and straight leg raise), hamstring stretch and gluteus strengthening	Mean Difference	-1.6 (-2.31, -0.89)	PRP treatment
Gaballa, 2019	Moderate	VAS Pain score	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Rehab: 3 sessions/wk for 4 successive wks; basic rehabilitation program including infrared (IR), trans cutaneous electric nerve stimulation (TENS), quadriceps muscle strengthening exercises (quadriceps setting and straight leg raise), hamstring stretch and gluteus strengthening	Mean Difference	-3.6 (-4.16, -3.04)	PRP treatment

Table 20: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Adverse Events

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Huang, 2019	Moderate	Deep Vein Thrombosis	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Infection	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Low-Grade Fever	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	RD	0.00(0.00,0.00)	NS
Huang, 2019	Moderate	Pain	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	RR	2.50(0.51,12.14)	NS

Table 21: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Adverse events

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2017	Moderate	Minor complications due to injection	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A, Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	RR	3.21(0.72,14.36)	NS
Raeissadat, 2017	Moderate	Injection-induced pain score	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A, Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	1.9 (0.82, 2.98)	Hyaluronic Acid treatment
Ahmad, 2018	High	Synovial vascularity	3 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-0.39 (-0.74, -0.04)	PRP treatment containing Leukocyte
Ahmad, 2018	High	Synovial hypertrophy	3 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-0.35 (-0.69, -0.01)	PRP treatment containing Leukocyte
Ahmad, 2018	High	Effusion	3 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	RR	0.49(0.25,0.97)	PRP treatment containing Leukocyte
Ahmad, 2018	High	Synovial vascularity	6 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-0.4 (-0.72, -0.08)	PRP treatment containing Leukocyte
Ahmad, 2018	High	Synovial hypertrophy	6 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-0.35 (-0.67, -0.03)	PRP treatment containing Leukocyte
Ahmad, 2018	High	Effusion	6 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	RR	0.39(0.17,0.92)	PRP treatment containing Leukocyte
Raeissadat, 2020	High	Minor complication due to injection	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, Abano Terme, Italy)	RR	3.47(1.01,11.87)	Hyaluronic Acid treatment
Vaquerizo, 2013	High	Any AE	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	RR	0.78(0.32,1.92)	NS
Park, 2021	High	System Organ Class AE	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	RR	0.75(0.28,2.02)	NS
Park, 2021	High	Injection Site Pain	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	RD	0.04(-0.01,0.09)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Park, 2021	High	Injection Site Swelling	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	RD	0.02(-0.02,0.05)	NS
Xu, 2021	High	Joint Swelling	. mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	RR	2.67(0.32,22.15)	NS
Xu, 2021	High	Pain after Injection	. mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	RD	0.17(0.03,0.30)	HA Injection

Table 22: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2015	High	WOMAC Total	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj.containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	-9.02 (-14.20, -3.84)	PRP treatment
Raeissadat, 2015	High	WOMAC Total	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj.containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Author Reported - Wilcoxon signed rank, Mann–Whitney, and Kruskal Wallis	N/A	NS
Raeissadat, 2015	High	WOMAC Total	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj.containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Author Reported - Wilcoxon signed rank, Mann–Whitney, and Kruskal Wallis	N/A	NS
Raeissadat, 2017	Moderate	WOMAC Total	2 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-1 (-6.77, 4.77)	NS
Raeissadat, 2017	Moderate	WOMAC Total	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-3 (-9.64, 3.64)	NS
Raeissadat, 2017	Moderate	LEQ Total	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	RR	1.58(0.89,2.81)	NS
Lin, 2019	High	WOMAC Total	1 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT;Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	0.62 (-9.15, 10.39)	NS
Lin, 2019	High	WOMAC Total	2 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT;Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	6.52 (-3.79, 16.83)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lin, 2019	High	WOMAC Total	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT;Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	9.38 (-0.41, 19.17)	NS
Lin, 2019	High	WOMAC Total	12 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT;Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	14.38 (3.69, 25.07)	Leukocyte-Poor Platelet Rich Plasma
Tavassoli, 2019	High	WOMAC Total	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	13.02(3.42,49.49)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.93(0.83,1.02)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.61(0.43,0.79)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.93(0.83,1.02)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	1.00(1.00,1.00)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.86(0.73,0.99)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.21(0.06,0.37)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.18(0.04,0.32)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.00(0.00,0.00)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.68(0.51,0.85)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.61(0.43,0.79)	PRP treatment
Tavassoli, 2019	High	WOMAC Total (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.25(0.09,0.41)	PRP treatment
Raeissadat, 2020	High	WOMAC Total	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-1.12 (-5.08, 2.84)	NS
Raeissadat, 2020	High	WOMAC Total	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-3.49 (-8.14, 1.16)	NS
Raeissadat, 2020	High	WOMAC Total	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-5.31 (-9.99, -0.63)	Platelets Rich in Growth Factors- PRGF
Raeissadat, 2020	High	LEQ Total	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-0.3 (-1.43, 0.83)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2020	High	LEQ Total	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-1.2 (-2.49, 0.09)	NS
Raeissadat, 2020	High	LEQ Total	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	Mean Difference	-1.4 (-2.65, -0.15)	Platelets Rich in Growth Factors- PRGF
Raeissadat, 2020	High	WOMAC Total (30% decrease)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	RR	3.12(1.84,5.28)	Platelets Rich in Growth Factors- PRGF
Raeissadat, 2020	High	LEQ Total	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A, AbanoTerme, Italy)	RR	2.86(0.97,8.39)	NS
Spakova, 2012	Moderate	WOMAC Total	13 wks	PRP treatment: 3 inj. In weekly intervals	Hyaluronic Acid treatment: HA (Erectus 1.2% CSC Pharmaceuticals Handels GmbH); 3 Inj. In weekly interval	Mean Difference	-11.82 (-17.51, -6.13)	PRP treatment
Spakova, 2012	Moderate	WOMAC Total	26 wks	PRP treatment: 3 inj. In weekly intervals	Hyaluronic Acid treatment: HA (Erectus 1.2% CSC Pharmaceuticals Handels GmbH); 3 Inj. In weekly interval	Mean Difference	-12.05 (-17.55, -6.55)	PRP treatment
Cerza, 2012	Moderate	WOMAC Total	4 wks	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP): mean injection 5mL; x1/week x 4 weeks	Hyaluronic Acid treatment: 20mg/2mL; x1/week x4 weeks	Mean Difference	-5.6 (-11.05, -0.15)	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP)
Cerza, 2012	Moderate	WOMAC Total	12 wks	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP): mean injection 5mL; x1/week x 4 weeks	Hyaluronic Acid treatment: 20mg/2mL; x1/week x4 weeks	Mean Difference	-17.9 (-23.29, -12.51)	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP)
Cerza, 2012	Moderate	WOMAC Total	24 wks	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP): mean injection 5mL; x1/week x 4 weeks	Hyaluronic Acid treatment: 20mg/2mL; x1/week x4 weeks	Mean Difference	-28.6 (-33.86, -23.34)	Platelet Rich Plasma (Autologous Conditioned Plasma, ACP)

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Buendia-Lopez,2018	High	WOMAC Total	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-3.72 (-4.30, -3.14)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Total	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-8.03 (-8.54, -7.52)	Leukocyte-Poor Platelet Rich Plasma
Huang, 2019	Moderate	WOMAC Total	3 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	Mean Difference	0.13 (-2.11, 2.37)	NS
Huang, 2019	Moderate	WOMAC Total	6 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	Mean Difference	-5.24 (-7.51, -2.97)	
Huang, 2019	Moderate	WOMAC Total	9 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	Mean Difference	-7.74 (-9.71, -5.77)	
Huang, 2019	Moderate	WOMAC Total	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	Mean Difference	-14.54 (-17.96, -11.12)	
Duymus, 2017	Moderate	WOMAC Total	1 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-6.8 (-12.03, -1.57)	PRP treatment
Duymus, 2017	Moderate	WOMAC Total	3 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-3.1 (-7.52, 1.32)	NS
Duymus, 2017	Moderate	WOMAC Total	6 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-1.7 (-4.98, 1.58)	NS
Duymus, 2017	Moderate	WOMAC Total	12 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-14.4 (-18.36, -10.44)	PRP treatment
Sanchez, 2012	High	WOMAC Total	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3injections on a weekly basis).	Mean Difference	-4.3 (-17.75, 9.15)	NS
Vaquerizo, 2013	High	WOMAC Total	24 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-23.2 (-31.03, -15.37)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	WOMAC Total	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-23.4 (-30.68, -16.12)	Platelets Rich in Growth Factors-PRGF

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Louis, M. L. 2018	High	WOMAC Total (WOMAC Scores)	3 mos	PRP treatment: single platelet-rich plasma (PRP) injection	Hyaluronic Acid treatment	Mean Difference	-2 (-15.83, 11.83)	NS
Park, 2021	High	WOMAC Total	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	4.6 (0.41, 8.79)	PRP injection
Park, 2021	High	WOMAC Total	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	4.5 (-0.81, 9.81)	NS
Park, 2021	High	WOMAC Total	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	-0.1 (-5.39, 5.19)	NS
Raeissadat, 2021	High	WOMAC Total	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.8 (-3.42, 1.82)	NS
Raeissadat, 2021	High	WOMAC Total	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-4.3 (-6.92, -1.68)	PRP injection
Raeissadat, 2021	High	WOMAC Total	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-7.1 (-9.65, -4.55)	PRP injection
Raeissadat, 2021	High	LEQ Total	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.2 (-0.58, 0.98)	NS
Raeissadat, 2021	High	LEQ Total	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.4 (-2.18, -0.62)	PRP injection
Raeissadat, 2021	High	LEQ Total	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.6 (-2.31, -0.89)	PRP injection
Bansal, 2021	High	WOMAC Total	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	NS
Bansal, 2021	High	WOMAC Total	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Total	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Total	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Total	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Su, K. 2018	Moderate	WOMAC Total (WOMAC Scores)	18 mos	intraosseous injection of PRP (group A)	Hyaluronic Acid treatment	Mean Difference	-10.47 (-11.98, -8.96)	intraosseous injection of PRP (group A)
Lisi, 2018	High	WOMAC Total	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Total	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Total	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Lysholm Scale Score	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lisi, 2018	High	Lysholm Scale Score	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Lysholm Scale Score	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Lequesne Index	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Lequesne Index	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Lequesne Index	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Buendia-Lopez,2018	High	WOMAC Total	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hrly	Mean Difference	-9.03 (-9.57, -8.49)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Total	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hrly	Mean Difference	-8.27 (-8.81, -7.73)	Leukocyte-Poor Platelet Rich Plasma

Table 23: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2015	High	WOMAC Function	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	-6.32 (-10.08, -2.56)	PRP treatment
Raeissadat, 2015	High	WOMAC Stiffness	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	-0.95 (-1.47, -0.43)	PRP treatment
Raeissadat, 2015	High	SF-36 Physical Function (physical health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	12.53 (3.48, 21.58)	PRP treatment
Raeissadat, 2015	High	SF-36 Physical Role Function (physical health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	20.52 (6.94, 34.10)	PRP treatment
Raeissadat, 2015	High	SF-36 Physical Component Summary (physical health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	66.57 (35.47, 97.67)	PRP treatment
Raeissadat, 2015	High	PCS-36 and MCS?36	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Author Reported - Wilcoxon signed rank, Mann–Whitney, and Kruskal Wallis	N/A	NS
Raeissadat, 2015	High	PCS-36 and MCS?36	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Author Reported - Wilcoxon signed rank, Mann–Whitney, and Kruskal Wallis	N/A	NS
Raeissadat, 2017	Moderate	WOMAC Function	2 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-1.1 (-5.31, 3.11)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2017	Moderate	WOMAC Stiffness	2 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	0.4 (-0.32, 1.12)	NS
Raeissadat, 2017	Moderate	WOMAC Function	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-2.5 (-7.15, 2.15)	NS
Raeissadat, 2017	Moderate	WOMAC Stiffness	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., Abano Terme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	0.2 (-0.59, 0.99)	NS
Lana, 2016	Moderate	WOMAC Stiffness	30 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Function	30 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Stiffness	90 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Function	90 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lana, 2016	Moderate	WOMAC Stiffness	180 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskal-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Function	180 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskal-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Stiffness	360 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskal-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	WOMAC Function	360 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskal-Wallis and Wilcoxon tests	N/A	PRP Treatment
Lin, 2019	High	IKDC	1 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	0.04 (-7.70, 7.78)	NS
Lin, 2019	High	IKDC	2 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	5.54 (-3.05, 14.13)	NS
Lin, 2019	High	IKDC	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	7.04 (-1.13, 15.21)	NS
Lin, 2019	High	IKDC	12 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Hyaluronic Acid treatment: 3 weekly intra-articular injections (2ml each time); of Hyruan Plus, 20 mg/2 mL; molecular weight > 2,500 kDa; LGChem, Seoul, Republic of Korea);	Mean Difference	11.29 (2.73, 19.85)	Leukocyte-Poor Platelet Rich Plasma
Ahmad, 2018	High	IKDC	3 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	8.3 (2.24, 14.36)	PRP treatment containing Leukocyte

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Ahmad, 2018	High	IKDC	6 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	10.1 (3.44, 16.76)	PRP treatment containing Leukocyte
Tavassoli, 2019	High	WOMAC Stiffness	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Stiffness	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Stiffness	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Stiffness	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Stiffness	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Stiffness	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Function (WOMAC Physical (PA))	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	N/A	PRP
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	1.57(1.13,2.18)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	1.42(1.03,1.95)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	3.66(1.60,8.41)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	12.54(3.29,47.76)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.82(0.68,0.96)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.43(0.25,0.61)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.41(0.22,0.59)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.37(0.19,0.55)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	4.82(2.16,10.75)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.93(0.83,1.02)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.93(0.83,1.02)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (30%decrease) (Patients having at least a 30% decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.82(0.68,0.96)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	2.05(1.07,3.94)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	1.93(0.99,3.75)	NS
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	6.75(0.89,51.27)	NS
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.18(0.04,0.32)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.18(0.04,0.32)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.04(-0.03,0.10)	NS
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	3.13(1.74,5.66)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	3.13(1.74,5.66)	PRP treatment
Tavassoli, 2019	High	WOMAC Stiffness (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	15.43(2.20,108.43)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.61(0.43,0.79)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.39(0.21,0.57)	PRP treatment
Tavassoli, 2019	High	WOMAC Function (50%decrease) (Patients having at least a 50% decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.18(0.04,0.32)	PRP treatment
Heredia, 2016	High	KOOS ADL	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	PRP
Heredia, 2016	High	KOOS ADL	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	PRP Treatment
Heredia, 2016	High	KOOS Sports/Rec	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	PRP Treatment
Heredia, 2016	High	KOOS Scores	Postop.	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EQ Mobility	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EQ Mobility	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EQ Daily Activity	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EQ Daily Activity	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2020	High	WOMAC Stiffness	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0.33 (-0.16, 0.82)	NS
Raeissadat, 2020	High	WOMAC Stiffness	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0.23 (-0.30, 0.76)	NS
Raeissadat, 2020	High	WOMAC Stiffness	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0.2 (-0.29, 0.69)	NS
Raeissadat, 2020	High	WOMAC Function (WOMAC Physical (PA))	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-1.03 (-3.93, 1.87)	NS
Raeissadat, 2020	High	WOMAC Function (WOMAC Physical (PA))	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-2.9 (-6.18, 0.38)	NS
Raeissadat, 2020	High	WOMAC Function (WOMAC Physical (PA))	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-4.61 (-7.97, -1.25)	Platelets Rich in Growth Factors-PRGF
Raeissadat, 2020	High	LEQ Walking (MWD, maximum walking distance)	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0 (-0.25, 0.25)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2020	High	LEQ ADL (ADL)	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.4 (-0.87, 0.07)	NS
Raeissadat, 2020	High	LEQ Walking (MWD, maximum walking distance)	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0 (-0.34, 0.34)	NS
Raeissadat, 2020	High	LEQ ADL (ADL)	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.7 (-1.20, -0.20)	Platelets Rich in Growth Factors-PRGF
Raeissadat, 2020	High	LEQ Walking (MWD, maximum walking distance)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0 (-0.40, 0.40)	NS
Raeissadat, 2020	High	LEQ ADL (ADL)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.6 (-1.07, -0.13)	Platelets Rich in Growth Factors-PRGF
Raeissadat, 2020	High	WOMAC Stiffness (30%decrease)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	RR	3.85(2.15,6.88)	Platelets Rich in Growth Factors-PRGF
Raeissadat, 2020	High	WOMAC Function (30%decrease) (Physical (PA))	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	RR	3.85(2.15,6.88)	Platelets Rich in Growth Factors-PRGF

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raecessadat, 2020	High	LEQ Walking (MWD, maximum walking distance)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	RR	0.96(0.87,1.06)	NS
Raecessadat, 2020	High	LEQ ADL (ADL)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy)	RR	5.72(1.33,24.53)	Platelets Rich in Growth Factors-PRGF
Buendia-Lopez,2018	High	WOMAC Function	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-6.44 (-6.81, -6.07)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-0.2 (-0.44, 0.04)	NS
Buendia-Lopez,2018	High	WOMAC Stiffness	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-0.58 (-0.78, -0.38)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Function, 20%Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	RD	0.24(0.10,0.39)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness, 20%Decrease	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	RR	2.91(1.20,7.07)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness, 20%Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	RD	0.27(0.12,0.42)	Leukocyte-Poor Platelet Rich Plasma
Duymus, 2017	Moderate	WOMAC Stiffness	1 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	0.1 (-0.36, 0.56)	NS
Duymus, 2017	Moderate	WOMAC Stiffness	3 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.2 (-0.70, 0.30)	NS
Duymus, 2017	Moderate	WOMAC Stiffness	6 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.2 (-0.64, 0.24)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Duymus, 2017	Moderate	WOMAC Stiffness	12 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.7 (-1.17, -0.23)	PRP treatment
Duymus, 2017	Moderate	WOMAC Function	1 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-4.6 (-8.61, -0.59)	PRP treatment
Duymus, 2017	Moderate	WOMAC Function	3 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-3.1 (-6.61, 0.41)	NS
Duymus, 2017	Moderate	WOMAC Function	6 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.5 (-3.23, 2.23)	NS
Duymus, 2017	Moderate	WOMAC Function	12 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-11 (-13.85, -8.15)	PRP treatment
Sanchez, 2012	High	Lequesne Index	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3 injections on a weekly basis).	Mean Difference	-0.2 (-1.19, 0.79)	NS
Sanchez, 2012	High	WOMAC Function	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3 injections on a weekly basis).	Mean Difference	-1.1 (-6.00, 3.80)	NS
Sanchez, 2012	High	WOMAC Stiffness	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3 injections on a weekly basis).	Mean Difference	-0.3 (-5.24, 4.64)	NS
Vaquerizo, 2013	High	WOMAC Stiffness	24 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-1.5 (-2.31, -0.69)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	WOMAC Function	24 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-16.5 (-22.20, -10.80)	Platelets Rich in Growth Factors-PRGF

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Vaquerizo, 2013	High	Lequesne Index	24 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-0.2 (-1.54, 1.14)	NS
Vaquerizo, 2013	High	WOMAC Stiffness	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-2.1 (-2.82, -1.38)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	WOMAC Function	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-17 (-22.35, -11.65)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	Lequesne Index	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-5.5 (-7.05, -3.95)	Platelets Rich in Growth Factors-PRGF
Gormeli, 2017	High	IKDC	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	12.4 (8.76, 16.04)	PRP treatment
Gormeli, 2017	High	IKDC; Early OA	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	16.2 (13.31, 19.09)	PRP treatment
Gormeli, 2017	High	IKDC; Advanced OA	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	4.2 (0.77, 7.63)	PRP treatment
Gormeli, 2017	High	IKDC	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	1.8 (-0.96, 4.56)	NS
Gormeli, 2017	High	IKDC; Early OA	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	1.7 (-1.39, 4.79)	NS
Gormeli, 2017	High	IKDC; Advanced OA	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	1.1 (-2.79, 4.99)	NS
Louis, M. L. 2018	High	WOMAC Stiffness (WOMAC Scores)	3 mos	PRP treatment: single platelet-rich plasma (PRP) injection	Hyaluronic Acid treatment	Mean Difference	0.2 (-1.18, 1.58)	NS
Louis, M. L. 2018	High	WOMAC Function (WOMAC Scores)	3 mos	PRP treatment: single platelet-rich plasma (PRP) injection	Hyaluronic Acid treatment	Mean Difference	-1.68 (-11.49, 8.13)	NS
Park, 2021	High	IKDC	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	1.9 (-1.94, 5.74)	NS
Park, 2021	High	IKDC	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	2.9 (-1.61, 7.41)	NS
Park, 2021	High	IKDC	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	5.2 (0.74, 9.66)	PRP injection
Park, 2021	High	WOMAC Function	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	3.2 (0.10, 6.30)	PRP injection
Park, 2021	High	WOMAC Function	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	2.8 (-0.97, 6.57)	NS
Park, 2021	High	WOMAC Function	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	-0.4 (-4.61, 3.81)	NS
Park, 2021	High	WOMAC Stiffness	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	0.7 (0.10, 1.30)	PRP injection
Park, 2021	High	WOMAC Stiffness	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	0.4 (-0.24, 1.04)	NS
Park, 2021	High	WOMAC Stiffness	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	0.1 (-0.55, 0.75)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Park, 2021	High	SMC Patellofemoral Function (Samsung Medical Center)	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	1.5 (-3.17, 6.17)	NS
Park, 2021	High	SMC Patellofemoral Function (Samsung Medical Center)	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	2.4 (-2.99, 7.79)	NS
Park, 2021	High	SMC Patellofemoral Function (Samsung Medical Center)	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	3.6 (-1.82, 9.02)	NS
Xu, 2021	High	Functional Scores	1 mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	Author Reported	N/A	NS
Xu, 2021	High	Functional Scores	6 mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	Author Reported	N/A	PRP
Xu, 2021	High	Functional Scores	12 mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	Author Reported	N/A	PRP
Xu, 2021	High	Functional Scores	24 mos	PRP injection: 3 injections/half month	HA Injection: 3 injections/half month	Author Reported	N/A	NS
Raeissadat, 2021	High	WOMAC Stiffness	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.2 (-0.16, 0.56)	NS
Raeissadat, 2021	High	WOMAC Stiffness	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0 (-0.36, 0.36)	NS
Raeissadat, 2021	High	WOMAC Stiffness	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.2 (-0.56, 0.16)	NS
Raeissadat, 2021	High	WOMAC Function	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.4 (-1.58, 2.38)	NS
Raeissadat, 2021	High	WOMAC Function	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.8 (-3.85, 0.25)	NS
Raeissadat, 2021	High	WOMAC Function	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-4.2 (-6.04, -2.36)	PRP injection
Raeissadat, 2021	High	LEQ Walking	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.04 (-0.22, 0.30)	NS
Raeissadat, 2021	High	LEQ Walking	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.12, 0.32)	NS
Raeissadat, 2021	High	LEQ Walking	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.09 (-0.34, 0.16)	NS
Raeissadat, 2021	High	LEQ ADL	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0 (-0.32, 0.32)	NS
Raeissadat, 2021	High	LEQ ADL	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.8 (-1.16, -0.44)	PRP injection
Raeissadat, 2021	High	LEQ ADL	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.7 (-1.02, -0.38)	PRP injection
Basnaev, 2021	Moderate	WOMAC Stiffness	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-9.7 (-18.06, -1.34)	PRP injection

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Basnaev, 2021	Moderate	WOMAC Stiffness	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-5.5 (-11.57, 0.57)	NS
Basnaev, 2021	Moderate	WOMAC Stiffness	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-4.4 (-10.16, 1.36)	NS
Basnaev, 2021	Moderate	WOMAC Function	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-1.6 (-12.22, 9.02)	NS
Basnaev, 2021	Moderate	WOMAC Function	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-17.7 (-25.03, -10.37)	PRP injection
Basnaev, 2021	Moderate	WOMAC Function	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-5 (-11.69, 1.69)	NS
Basnaev, 2021	Moderate	Lequesne Index	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-1.3 (-1.41, -1.19)	PRP injection
Basnaev, 2021	Moderate	Lequesne Index	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-0.4 (-0.51, -0.29)	PRP injection
Basnaev, 2021	Moderate	Lequesne Index	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-1.4 (-1.57, -1.23)	PRP injection
Bansal, 2021	High	WOMAC Stiffness	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	NS
Bansal, 2021	High	WOMAC Stiffness	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Stiffness	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Stiffness	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Stiffness	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Function	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Function	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Function	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Function	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Function	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	IKDC	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Mean Difference	3.15 (0.81, 5.49)	PRP injection

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Bansal, 2021	High	IKDC	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Mean Difference	19.38 (16.49, 22.27)	PRP injection
Bansal, 2021	High	IKDC	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Mean Difference	14.1 (12.14, 16.06)	PRP injection
Bansal, 2021	High	IKDC	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Mean Difference	10.1 (7.85, 12.35)	PRP injection
Bansal, 2021	High	IKDC	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Mean Difference	10.1 (7.95, 12.25)	PRP injection
Bansal, 2021	High	Pain Free Distance During 6MWT	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	Pain Free Distance During 6MWT	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	Pain Free Distance During 6MWT	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	Pain Free Distance During 6MWT	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	Pain Free Distance During 6MWT	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Su, K. 2018	Moderate	WOMAC Stiffness (WOMAC Scores)	18 mos	intraosseous injection of PRP (group A)	Hyaluronic Acid treatment	Mean Difference	-0.83 (-1.13, -0.53)	intraosseous injection of PRP (group A)
Su, K. 2018	Moderate	WOMAC Function (WOMAC Scores)	18 mos	intraosseous injection of PRP (group A)	Hyaluronic Acid treatment	Mean Difference	-7.91 (-9.17, -6.65)	intraosseous injection of PRP (group A)
Cole, 2017	High	IKDC	1 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	5 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	9 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	13 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	17 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	21 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	24 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	PRP
Cole, 2017	High	IKDC	25 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Cole, 2017	High	IKDC	29 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	33 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	37 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	41 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	45 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	49 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	IKDC	52 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Lisi, 2018	High	WOMAC Stiffness	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Stiffness	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Stiffness	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC ADL	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC ADL	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	PRP
Lisi, 2018	High	WOMAC ADL	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	PRP
Lisi, 2018	High	AKSS	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lisi, 2018	High	AKSS	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	AKSS	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Tegner Scale	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Tegner Scale	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	Tegner Scale	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Buendia-Lopez,2018	High	WOMAC Function	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hourly	Mean Difference	-6.57 (-6.94, -6.20)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hourly	Mean Difference	-0.82 (-1.04, -0.60)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hourly	Mean Difference	-0.82 (-1.05, -0.59)	Leukocyte-Poor Platelet Rich Plasma

Table 24: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2015	High	WOMAC Pain	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 winterly); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	-1.05 (-2.24, 0.14)	NS
Raeissadat, 2015	High	SF-36 Bodily Pain (physical health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 winterly); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	23.55 (15.35, 31.75)	PRP treatment
Raeissadat, 2017	Moderate	WOMAC Pain	2 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-0.1 (-1.42, 1.22)	NS
Raeissadat, 2017	Moderate	WOMAC Pain	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-0.6 (-2.11, 0.91)	NS
Raeissadat, 2017	Moderate	VAS Pain score	2 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	0.1 (-0.85, 1.05)	NS
Raeissadat, 2017	Moderate	VAS Pain score	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	Mean Difference	-0.2 (-1.42, 1.02)	NS
Raeissadat, 2017	Moderate	LEQ Pain	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, FidiaFarmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	RR	3.21(0.72,14.36)	NS
Lana, 2016	Moderate	VAS Pain score	30 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lana, 2016	Moderate	WOMAC Pain	30 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	VAS Pain score	90 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	PRP Treatment
Lana, 2016	Moderate	WOMAC Pain	90 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	VAS Pain score	180 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	PRP Treatment
Lana, 2016	Moderate	WOMAC Pain	180 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Lana, 2016	Moderate	VAS Pain score	360 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	PRP Treatment
Lana, 2016	Moderate	WOMAC Pain	360 days	PRP treatment: 3 inj.in 2 wks interval; Activation with autologous thrombin, in the proportion of 0.8 ml of thrombin for 5 ml of PRP. Lidocaine 2% with epinephrine	Hyaluronic Acid treatment: 3 inj.in 2 wks interval (2.0 ml (20 mg of HA) of high molecular weight (2.4 - 3.6 million daltons) non cross-linked hyaluronic acid extracted from bacteria cells (Eufflexa-Ferring 10mg/ml HA)	Author Reported - Kruskall-Wallis and Wilcoxon tests	N/A	NS
Ahmad, 2018	High	VAS Pain score	3 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-0.7 (-1.36, -0.04)	PRP treatment containing Leukocyte

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Ahmad, 2018	High	VAS Pain score	6 mos	PRP treatment containing Leukocyte: 3 inj. at 2 weeks interval;	Hyaluronic Acid treatment: 3 inj. at 2 weeks interval; 2.0 mL (20 mg of HA) of high molecular weight HA	Mean Difference	-1.81 (-2.43, -1.19)	PRP treatment containing Leukocyte
Tavassoli, 2019	High	WOMAC Pain	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - paired t-test, independent t-test and ANOVA test	N/A	PRP
Tavassoli, 2019	High	VAS Pain score	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP
Tavassoli, 2019	High	VAS Pain score	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP
Tavassoli, 2019	High	VAS Pain score	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP
Tavassoli, 2019	High	VAS Pain score	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	VAS Pain score	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP
Tavassoli, 2019	High	VAS Pain score	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	Author Reported - chi-square test	N/A	PRP
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.78(0.62,0.93)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	5.21(2.35,11.52)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.86(0.73,0.99)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.78(0.62,0.93)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.81(0.67,0.96)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (30% decrease) (Patients having at least a 30%decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	1.00(1.00,1.00)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.50(0.31,0.69)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.39(0.21,0.57)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.21(0.06,0.37)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.89(0.78,1.01)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.82(0.68,0.96)	PRP treatment
Tavassoli, 2019	High	WOMAC Pain (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.57(0.39,0.75)	PRP treatment
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	5.46(1.80,16.54)	PRP treatment
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	5.30(1.29,21.74)	PRP treatment
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: single inj. of PRP	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.07(-0.02,0.17)	NS
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	4 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	0.89(0.77,1.01)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	8 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RR	12.05(3.16,46.02)	PRP treatment
Tavassoli, 2019	High	VAS Pain score (50% decrease) (Patients having at least a 50%decrease in the summed score for the scales)	12 wks	PRP treatment: two inj. of PRP; 2nd inj. After an interval of 2 wks	Hyaluronic Acid treatment: 3 inj. of Hyalgan at 1 week interval; contains high molecular weight (500-730 kilodalton) fraction of purified sodium hyaluronate (30 mg/2 mL).	RD	0.61(0.43,0.79)	PRP treatment
Heredia, 2016	High	KOOS Pain	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	PRP Treatment
Heredia, 2016	High	EQ Pain	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EQ Pain	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Heredia, 2016	High	EURO QOL Pain Scale-Worsening (After 3rd infiltration)	Postop.	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	7.4 (0.00, 14.80)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Similar (After 3rd infiltration)	Postop.	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	8.7 (-90.13, 107.53)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Improvement (After 3rdinfiltration)	Postop.	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	-16.1 (-55.34, 23.14)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Worsening (3 months after 3rdinfiltration)	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	-7.8 (-19.88, 4.28)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Similar (3months after 3rd infiltration)	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	-5.7 (-77.87, 66.47)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Improvement (3 months after 3rdinfiltration)	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	13.5 (-45.75, 72.75)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Worsening (6 months after 3rdinfiltration)	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	-8 (-25.09, 9.09)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Similar (6months after 3rd infiltration)	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	-1.9 (-71.28, 67.48)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Improvement (6 months after 3rdinfiltration)	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Mean Difference	9.8 (-46.49, 66.09)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Heredia, 2016	High	VAS Pain score (50% decrease) (After 3rd infiltration)	Postop.	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	RR	0.96(0.60,1.54)	NS
Heredia, 2016	High	VAS Pain score (50% decrease) (3 months after 3rd infiltration)	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	RR	1.81(0.93,3.52)	NS
Heredia, 2016	High	VAS Pain score (50% decrease) (6 months after 3rd infiltration)	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	RR	1.05(0.57,1.94)	NS
Raeissadat, 2020	High	WOMAC Pain	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.33 (-1.28, 0.62)	NS
Raeissadat, 2020	High	WOMAC Pain	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.68 (-1.73, 0.37)	NS
Raeissadat, 2020	High	WOMAC Pain	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.83 (-1.84, 0.18)	NS
Raeissadat, 2020	High	VAS Pain score	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.2 (-0.91, 0.51)	NS
Raeissadat, 2020	High	VAS Pain score	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.4 (-1.22, 0.42)	NS
Raeissadat, 2020	High	VAS Pain score	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-1.6 (-2.28, -0.92)	Platelets Rich in Growth Factors-PRGF

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2020	High	LEQ Pain	2 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	0.1 (-0.45, 0.65)	NS
Raeissadat, 2020	High	LEQ Pain	6 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.4 (-1.02, 0.22)	NS
Raeissadat, 2020	High	LEQ Pain	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	Mean Difference	-0.8 (-1.36, -0.24)	Platelets Rich in Growth Factors-PRGF
Raeissadat, 2020	High	WOMAC Pain (30% decrease)	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	RR	0.91(0.71,1.16)	NS
Raeissadat, 2020	High	LEQ Pain	12 mos	Platelets Rich in Growth Factors- PRGF: 8 mL of plasma with 4.6± 0.7times more than the platelet concentration + 1.5 mL of platelet-activating factor (Rooyagen); "platelet-rich plasma (PRP)-derived growth factor (PRGF)"containing epinephrine and calcium chloride (25mmol/l)	Hyaluronic Acid treatment: three injections of HA weekly (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy)	RR	2.39(1.27,4.50)	Hyaluronic Acid treatment
Spakova, 2012	Moderate	VAS Pain score	13 wks	PRP treatment: 3 inj. In weekly intervals	Hyaluronic Acid treatment: HA (Erectus 1.2% CSC Pharmaceuticals Handels GmbH); 3 Inj. In weekly interval	Mean Difference	-1.92 (-2.69, -1.15)	PRP treatment
Spakova, 2012	Moderate	VAS Pain score	26 wks	PRP treatment: 3 inj. In weekly intervals	Hyaluronic Acid treatment: HA (Erectus 1.2% CSC Pharmaceuticals Handels GmbH); 3 Inj. In weekly interval	Mean Difference	-1.61 (-2.31, -0.91)	PRP treatment
Buendia-Lopez,2018	High	VAS Pain score	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-0.31 (-0.58, -0.04)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-0.43 (-0.85, -0.01)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	Mean Difference	-1.12 (-1.40, -0.84)	Leukocyte-Poor Platelet Rich Plasma

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Buendia-Lopez,2018	High	WOMAC Pain, 20% Decrease	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	RR	2.22(1.05,4.66)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain, 20% Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Hyaluronic Acid treatment: 60 mg/2 mL for 52 weeks	RD	0.30(0.15,0.46)	Leukocyte-Poor Platelet Rich Plasma
Huang, 2019	Moderate	VAS Pain score	12 mos	4 ml three times every three weeks	Hyaluronic Acid treatment: 2 ml per week for three weeks	Mean Difference	-0.16 (-0.81, 0.49)	NS
Duymus, 2017	Moderate	VAS Pain score	1 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.6 (-0.99, -0.21)	PRP treatment
Duymus, 2017	Moderate	VAS Pain score	3 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.2 (-0.59, 0.19)	NS
Duymus, 2017	Moderate	VAS Pain score	6 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.3 (-0.92, 0.32)	NS
Duymus, 2017	Moderate	VAS Pain score	12 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-1.7 (-2.14, -1.26)	PRP treatment
Duymus, 2017	Moderate	WOMAC Pain	1 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	0.7 (-0.31, 1.71)	NS
Duymus, 2017	Moderate	WOMAC Pain	3 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	0.24 (-0.76, 1.24)	NS
Duymus, 2017	Moderate	WOMAC Pain	6 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-0.3 (-1.09, 0.49)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Duymus, 2017	Moderate	WOMAC Pain	12 mos	PRP treatment: 2 injections per month	Hyaluronic Acid treatment: 1 Injection (Ostenil Plus® syringe is a pre-filled syringe containing 40 mg of fermentative HA and 10 mg of mannitol, molecular weight 1.6 Million Daltons)	Mean Difference	-2.8 (-3.70, -1.90)	PRP treatment
Sanchez, 2012	High	WOMAC Pain	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3injections on a weekly basis).	Mean Difference	-2.8 (-7.43, 1.83)	NS
Sanchez, 2012	High	WOMAC Pain, 20% Decrease	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3injections on a weekly basis).	RR	1.08(0.83,1.42)	NS
Sanchez, 2012	High	WOMAC Pain, 50% Decrease	24 wks	Platelets Rich in Growth Factors- PRGF: PRGF-Endoret (3injectionson a weekly basis); 8ml of plasma (rich in platelets) activated before infiltration, by adding 400 mL of calcium chloride	Hyaluronic Acid treatment: HA (Euflexxa; Copenhagen, Denmark) (3injections on a weekly basis).	RR	1.58(1.00,2.50)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	WOMAC Pain	24 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-5.3 (-6.92, -3.68)	Platelets Rich in Growth Factors-PRGF
Vaquerizo, 2013	High	WOMAC Pain	48 wks	Platelets Rich in Growth Factors- PRGF: 8mL 1 injection/2weeks x3injections	Hyaluronic Acid treatment: Hyaluronic Acid (Durolane); 60mg/3mLSingle injection	Mean Difference	-4.4 (-5.74, -3.06)	Platelets Rich in Growth Factors-PRGF
Gormeli, 2017	High	EQ Pain	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	10.6 (6.53, 14.67)	PRP treatment
Gormeli, 2017	High	EQ-VAS; Early OA	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	14.2 (11.19, 17.21)	PRP treatment
Gormeli, 2017	High	EQ-VAS; Advanced OA	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	2.7 (-0.94, 6.34)	NS
Gormeli, 2017	High	EQ Pain	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	1.2 (-1.71, 4.11)	NS
Gormeli, 2017	High	EQ-VAS; Early OA	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	0.7 (-2.19, 3.59)	NS
Gormeli, 2017	High	EQ-VAS; Advanced OA	6 mos	PRP treatment: PRP injection 1 time	Hyaluronic Acid treatment: HA injection 3 times	Mean Difference	1.3 (-2.67, 5.27)	NS
Louis, M. L. 2018	High	WOMAC Pain (WOMAC Scores)	3 mos	PRP treatment: single platelet-rich plasma (PRP) injection	Hyaluronic Acid treatment	Mean Difference	-0.5 (-3.76, 2.76)	NS
Louis, M. L. 2018	High	VAS Pain score	3 mos	PRP treatment: single platelet-rich plasma (PRP) injection	Hyaluronic Acid treatment	Mean Difference	-0.2 (-2.09, 1.69)	NS
Park, 2021	High	VAS Pain score	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	5.2 (-1.17, 11.57)	NS
Park, 2021	High	VAS Pain score	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	4 (-3.40, 11.40)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Park, 2021	High	VAS Pain score	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	7.3 (0.12, 14.48)	HA injection
Park, 2021	High	WOMAC Pain	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	0.7 (-0.40, 1.80)	NS
Park, 2021	High	WOMAC Pain	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	1.3 (-0.38, 2.98)	NS
Park, 2021	High	WOMAC Pain	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	0.2 (-0.94, 1.34)	NS
Park, 2021	High	SMC Patellofemoral Pain (Samsung Medical Center)	6 wks	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	2.4 (-2.11, 6.91)	NS
Park, 2021	High	SMC Patellofemoral Pain (Samsung Medical Center)	3 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	5.1 (-0.10, 10.30)	NS
Park, 2021	High	SMC Patellofemoral Pain (Samsung Medical Center)	6 mos	PRP injection: Single injection; leukocyte rich	HA injection: 3 mL	Mean Difference	4.1 (-1.35, 9.55)	NS
Raeissadat, 2021	High	WOMAC Pain	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.5 (-1.14, 0.14)	NS
Raeissadat, 2021	High	WOMAC Pain	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1 (-1.64, -0.36)	PRP injection
Raeissadat, 2021	High	WOMAC Pain	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.3 (-1.80, -0.80)	PRP injection
Raeissadat, 2021	High	LEQ Pain	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.6 (0.18, 1.02)	HA Injection
Raeissadat, 2021	High	LEQ Pain	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.1 (-0.52, 0.32)	NS
Raeissadat, 2021	High	LEQ Pain	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.4 (-0.82, 0.02)	NS
Raeissadat, 2021	High	VAS Pain score	2 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.47, 0.67)	NS
Raeissadat, 2021	High	VAS Pain score	6 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.4 (-0.90, 0.10)	NS
Raeissadat, 2021	High	VAS Pain score	12 mos	PRP injection: 2 doses/3 weeks	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.7 (-1.20, -0.20)	PRP injection
Basnaev, 2021	Moderate	VAS Pain score	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	0.5 (0.35, 0.65)	HA injection
Basnaev, 2021	Moderate	VAS Pain score	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-0.6 (-0.67, -0.53)	PRP injection
Basnaev, 2021	Moderate	VAS Pain score	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-1.2 (-1.31, -1.09)	PRP injection
Basnaev, 2021	Moderate	VAS Pain During Walking	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	0.4 (0.27, 0.53)	HA injection
Basnaev, 2021	Moderate	VAS Pain During Walking	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-0.5 (-0.57, -0.43)	PRP injection

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Basnaev, 2021	Moderate	VAS Pain During Walking	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-0.5 (-0.57, -0.43)	PRP injection
Basnaev, 2021	Moderate	WOMAC Pain	1 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	15.4 (6.40, 24.40)	HA injection
Basnaev, 2021	Moderate	WOMAC Pain	3 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-14.53 (-22.32, -6.74)	PRP injection
Basnaev, 2021	Moderate	WOMAC Pain	6 mos	PRP injection: 4 PRP injections; 1/wk for 4 mos	HA injection: IA inj 1/wk for 1 month	Mean Difference	-3.26 (-9.00, 2.48)	NS
Bansal, 2021	High	WOMAC Pain	1 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	NS
Bansal, 2021	High	WOMAC Pain	3 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Pain	6 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Pain	9 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Bansal, 2021	High	WOMAC Pain	12 mos	PRP injection: 1 8mL IA injection	HA injection: 4mL HA IA	Author Reported	N/A	PRP
Su, K. 2018	Moderate	VAS Pain score	18 mos	intraosseous injection of PRP (group A)	Hyaluronic Acid treatment	Mean Difference	-2.76 (-2.92, -2.60)	intraosseous injection of PRP (group A)
Su, K. 2018	Moderate	WOMAC Pain (WOMAC Scores)	18 mos	intraosseous injection of PRP (group A)	Hyaluronic Acid treatment	Mean Difference	-2.17 (-2.49, -1.85)	intraosseous injection of PRP (group A)
Cole, 2017	High	VAS Pain score	1 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Mean Difference	-0.98 (-5.99, 4.03)	NS
Cole, 2017	High	VAS Pain score	5 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	9 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	13 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	17 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	21 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	24 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	PRP

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Cole, 2017	High	VAS Pain score	25 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	29 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	33 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	37 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	41 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	45 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	49 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	NS
Cole, 2017	High	VAS Pain score	52 wks	PRP treatment: 3 Treatments for 3 weeks	IA HA: 3 Treatments for 3 weeks	Author Reported - Author Reported; from graph	N/A	PRP
Lisi, 2018	High	VAS Pain score	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	VAS Pain score	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	VAS Pain score	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Pain	12 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Pain	15 days	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS
Lisi, 2018	High	WOMAC Pain	6 mos	PRP treatment: three autologous activated platelet-rich plasma plus calcium gluconate (as activator) intra-articular injections at four week intervals	Hyaluronic Acid treatment: three intraarticular hyaluronic acid (20 mg/2mL) injections at 4 week intervals	Author Reported - Author Reported	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Buendia-Lopez,2018	High	WOMAC Pain	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hourly	Mean Difference	-1.03 (-1.36, -0.70)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Oral NSAID: oral diclofenac 75MG 12 hourly	Mean Difference	-0.88 (-1.17, -0.59)	Leukocyte-Poor Platelet Rich Plasma

Table 25: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid- QOL

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2015	High	SF-36 General Health perception (physical health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	7.87 (0.01, 15.73)	PRP treatment
Raeissadat, 2015	High	SF-36 Vitality (mental health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	8.53 (-0.28, 17.34)	NS
Raeissadat, 2015	High	SF-36 Social Functioning (mental health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	16.08 (6.65, 25.51)	PRP treatment
Raeissadat, 2015	High	SF-36 Emotional Role Function (mental health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	0 (-13.05, 13.05)	NS
Raeissadat, 2015	High	SF-36 Mental Health (mental health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	13.8 (5.50, 22.10)	PRP treatment
Raeissadat, 2015	High	SF-36 Mental Component Summary (mental health dimension)	52 wks	PRP treatment: 4–6 mL of PRP containing leukocytes (2 inj. 4 wks interval); single dose of acetaminophen-codeine 2 hours before the injection given instead of LA; platelets activated by direct contact with joint collagen;	Hyaluronic Acid treatment: 3 doses at 1-week interval; 2ml Hylgan inj. containing 20 mg of sodium hyaluronate, 17 mg of sodium chloride,	Mean Difference	53.01 (20.63, 85.39)	PRP treatment
Raeissadat, 2017	Moderate	Lequesne scale scores- walk	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.P.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	RR	1.22(0.59,2.52)	NS
Raeissadat, 2017	Moderate	Lequesne scale scores- daily life	6 mos	Platelets Rich in Growth Factors- PRGF: 5ml inj. Within 20 min of preparation; Acetaminophen given 2 hrs prior to inj. Instead of giving LA.	Hyaluronic Acid treatment: 3 weekly inj. by HA (Hyalgan, Fidia Farmaceutici S.p.A., AbanoTerme, Italy); syringe contained 20 mg of the active ingredient sodium hyaluronate in 2 mL of liquid with mol wt. of 500 to 730 kDa	RR	2.38(0.95,5.96)	NS
Heredia, 2016	High	EQ Personal Care	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Heredia, 2016	High	EQ Personal Care	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Hyaluronic Acid treatment: 2.5 mL sodium hyaluronate (25 mg)	Author Reported - Wilcoxon test	N/A	NS
Di Martino, 2019	High	EQ (VAS)	2 mos	Leukocyte rich PRP: 3weekly intra-articular injections of leukocyte-rich PRP	Hyaluronic Acid treatment: 3 weekly administrations of high-molecular-weight HA (Hyalubrix 30 mg/2 mL, molecularweight.1500KDa; Fidia SPA)	Mean Difference	1.9 (-1.97, 5.77)	NS
Di Martino, 2019	High	EQ (VAS)	6 mos	Leukocyte rich PRP: 3weekly intra-articular injections of leukocyte-rich PRP	Hyaluronic Acid treatment: 3 weekly administrations of high-molecular-weight HA (Hyalubrix 30 mg/2 mL, molecularweight.1500KDa; Fidia SPA)	Mean Difference	3.1 (-1.16, 7.36)	NS
Di Martino, 2019	High	EQ (VAS)	12 mos	Leukocyte rich PRP: 3weekly intra-articular injections of leukocyte-rich PRP	Hyaluronic Acid treatment: 3 weekly administrations of high-molecular-weight HA (Hyalubrix 30 mg/2 mL, molecularweight.1500KDa; Fidia SPA)	Mean Difference	5.1 (1.11, 9.09)	Leukocyte rich PRP
Di Martino, 2019	High	EQ (VAS)	24 mos	Leukocyte rich PRP: 3weekly intra-articular injections of leukocyte-rich PRP	Hyaluronic Acid treatment: 3 weekly administrations of high-molecular-weight HA (Hyalubrix 30 mg/2 mL, molecularweight.1500KDa; Fidia SPA)	Mean Difference	5.1 (0.40, 9.80)	Leukocyte rich PRP

Table 26: PICO 1f- 1: Platelet rich plasma vs. 1: Hyaluronic acid +PRP- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2021	High	WOMAC Total	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.1 (-3.94, 1.74)	NS
Raeissadat, 2021	High	WOMAC Total	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-4.7 (-7.62, -1.78)	PRGF
Raeissadat, 2021	High	WOMAC Total	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-7.5 (-10.36, -4.64)	PRGF
Raeissadat, 2021	High	LEQ Total	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.4 (-0.38, 1.18)	NS
Raeissadat, 2021	High	LEQ Total	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.3 (-2.08, -0.52)	PRGF
Raeissadat, 2021	High	LEQ Total	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.4 (-2.26, -0.54)	PRGF

Table 27: PICO 1f- 1: Platelet richplasma vs. 1:Hyaluronic acid +PRP- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2021	High	WOMAC Stiffness	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.2 (-0.27, 0.67)	NS
Raeissadat, 2021	High	WOMAC Stiffness	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0 (-0.54, 0.54)	NS
Raeissadat, 2021	High	WOMAC Stiffness	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.16 (-0.57, 0.25)	NS
Raeissadat, 2021	High	WOMAC Function	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-2.04, 2.24)	NS
Raeissadat, 2021	High	WOMAC Function	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-2.3 (-4.50, -0.10)	PRGF
Raeissadat, 2021	High	WOMAC Function	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-4.7 (-6.90, -2.50)	PRGF
Raeissadat, 2021	High	LEQ Walking	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.18, 0.38)	NS
Raeissadat, 2021	High	LEQ Walking	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.12, 0.32)	NS
Raeissadat, 2021	High	LEQ Walking	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.04 (-0.31, 0.23)	NS
Raeissadat, 2021	High	LEQ ADL	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.22, 0.42)	NS
Raeissadat, 2021	High	LEQ ADL	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.8 (-1.16, -0.44)	PRGF
Raeissadat, 2021	High	LEQ ADL	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.7 (-1.02, -0.38)	PRGF

Table 28: PICO 1f- 1: Platelet richplasma vs. 1:Hyaluronic acid +PRP- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2021	High	WOMAC Pain	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.5 (-1.22, 0.22)	NS
Raeissadat, 2021	High	WOMAC Pain	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1 (-1.72, -0.28)	PRGF
Raeissadat, 2021	High	WOMAC Pain	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-1.3 (-1.97, -0.63)	PRGF
Raeissadat, 2021	High	LEQ Pain	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.6 (0.10, 1.10)	HA Injection
Raeissadat, 2021	High	LEQ Pain	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.1 (-0.60, 0.40)	NS
Raeissadat, 2021	High	LEQ Pain	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.3 (-0.72, 0.12)	NS
Raeissadat, 2021	High	VAS Pain score	2 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	0.1 (-0.47, 0.67)	NS
Raeissadat, 2021	High	VAS Pain score	6 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.3 (-0.80, 0.20)	NS
Raeissadat, 2021	High	VAS Pain score	12 mos	PRGF: 2 doses with 3 wk intervals	HA Injection: 1 injection/week for 3 wks	Mean Difference	-0.8 (-1.30, -0.30)	PRGF

Table 29: PICO 1h- 1: Platelet rich plasma vs. 1: Placebo- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lin, 2019	High	WOMAC Total	1 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	6.65 (-2.25, 15.55)	NS
Lin, 2019	High	WOMAC Total	2 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	14.05 (4.94, 23.16)	Leukocyte-Poor Platelet Rich Plasma
Lin, 2019	High	WOMAC Total	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	12.58 (3.68, 21.48)	Leukocyte-Poor Platelet Rich Plasma
Lin, 2019	High	WOMAC Total	12 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	16.77 (7.14, 26.40)	Leukocyte-Poor Platelet Rich Plasma
Wu, 2018	High	WOMAC Total	2 wks	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-2.6 (-6.52, 1.32)	NS
Wu, 2018	High	WOMAC Total	1 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-3.9 (-7.26, -0.54)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Total	3 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-14.2 (-16.31, -12.09)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Total	6 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-6.9 (-9.08, -4.72)	leukocyte and platelet-rich plasma
Patel. 2013	High	WOMAC Total	6 wks	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Total	3 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Total	6 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Patel. 2013	High	WOMAC Total	6 wks	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Total	3 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Total	6 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Ghai, B. 2019	High	WOMAC Total	1 mos	PRP treatment	Normal saline: NS	Mean Difference	1 (-16.29, 18.29)	NS
Ghai, B. 2019	High	WOMAC Total	1.5 mos	PRP treatment	Normal saline: NS	Mean Difference	1 (-2.45, 4.45)	NS
Ghai, B. 2019	High	WOMAC Total	3 mos	PRP treatment	Normal saline: NS	Mean Difference	-8.65 (-14.87, -2.43)	PRP treatment
Ghai, B. 2019	High	WOMAC Total	6 mos	PRP treatment	Normal saline: NS	Mean Difference	-8.35 (-15.40, -1.30)	PRP treatment
Eroglu, 2016	Moderate	WOMAC Total (Before 2 nd injection)	Postop .	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	0.15 (-8.58, 8.88)	NS
Eroglu, 2016	Moderate	WOMAC Total	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-1.39 (-9.81, 7.03)	NS
Eroglu, 2016	Moderate	WOMAC Total	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.99 (-9.17, 7.19)	NS
Elik, H. 2020	High	WOMAC Total (WOMAC Scores)	1 mos	PRP treatment	Placebo	Mean Difference	-8.16 (-17.41, 1.09)	NS
Elik, H. 2020	High	WOMAC Total (WOMAC Scores)	6 mos	PRP treatment	Placebo	Mean Difference	-17.5 (-27.23, -7.77)	PRP treatment
Smith, P. A.2016	High	WOMAC Total (WOMACosteoarthritis Index Scores)	1 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-3 (-12.43, 6.43)	NS
Smith, P. A.2016	High	WOMAC Total (WOMACosteoarthritis Index Scores)	2 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-14 (-24.63, -3.37)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Total (WOMACosteoarthritis Index Scores)	2 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-17 (-30.45, -3.55)	Intra-articular Autologous Conditioned Plasma Injections

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Smith, P. A.2016	High	WOMAC Total (WOMAC Osteoarthritis Index Scores)	3 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-27 (-38.31, -15.69)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Total (WOMAC Osteoarthritis Index Scores)	6 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-33 (-45.73, -20.27)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Total (WOMAC Osteoarthritis Index Scores)	12 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-33 (-46.04, -19.96)	Intra-articular Autologous Conditioned Plasma Injections

Table 30: PICO 1h- 1: Platelet rich plasma vs. 1: Placebo- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Lin, 2019	High	IKDC	1 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	4.96 (-1.73, 11.65)	NS
Lin, 2019	High	IKDC	2 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	12.27 (5.24, 19.30)	Leukocyte-Poor Platelet Rich Plasma
Gormeli, 2017	High	IKDC	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Normal saline: 3 saline injections	Mean Difference	24.3 (20.88, 27.72)	PRP treatment
Gormeli, 2017	High	IKDC	6 mos	PRP treatment: PRP injection 1 time	Normal saline: 3 saline injections	Mean Difference	13.7 (11.22, 16.18)	PRP treatment
Lin, 2019	High	IKDC	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	13.13 (5.99, 20.27)	Leukocyte-Poor Platelet Rich Plasma
Lin, 2019	High	IKDC	12 mos	Leukocyte-Poor Platelet Rich Plasma: 3 weekly intra-articular injections (2ml each time); PRP (RegenKit-THT; Regen Lab, LeMont-sur-Lausanne, Switzerland)	Normal Saline: 3 weekly intra-articular injections (2ml each time)	Mean Difference	16.97 (9.44, 24.50)	Leukocyte-Poor Platelet Rich Plasma
Wu, 2018	High	WOMAC Stiffness	2 wks	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-0.7 (-1.11, -0.29)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Stiffness	1 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-0.7 (-1.10, -0.30)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Stiffness	3 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-1.4 (-1.72, -1.08)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Stiffness	6 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-0.7 (-1.04, -0.36)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Function (WOMAC Physical (PA))	2 wks	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	1 (-1.76, 3.76)	NS
Wu, 2018	High	WOMAC Function (WOMAC Physical (PA))	1 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-1 (-3.33, 1.33)	NS
Wu, 2018	High	WOMAC Function (WOMAC Physical (PA))	3 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-7.6 (-9.15, -6.05)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Function (WOMAC Physical (PA))	6 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-2.8 (-4.39, -1.21)	leukocyte and platelet-rich plasma
Patel. 2013	High	WOMAC Stiffness	6 wks	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Patel. 2013	High	WOMAC Stiffness	3 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Stiffness	6 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	6 wks	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	3 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	6 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Stiffness	6 wks	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Stiffness	3 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Stiffness	6 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	6 wks	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	3 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Function (WOMAC Physical (PA))	6 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA) followed by post hoc tests	N/A	PRP
Ghai, B. 2019	High	WOMAC Stiffness	1 mos	PRP treatment	Normal saline: NS	Mean Difference	0.1 (-0.36, 0.56)	NS
Ghai, B. 2019	High	WOMAC Stiffness	1.5 mos	PRP treatment	Normal saline: NS	Mean Difference	0.1 (-0.47, 0.67)	NS
Ghai, B. 2019	High	WOMAC Stiffness	3 mos	PRP treatment	Normal saline: NS	Mean Difference	-1.4 (-2.37, -0.43)	PRP treatment
Ghai, B. 2019	High	WOMAC Stiffness	6 mos	PRP treatment	Normal saline: NS	Mean Difference	-1.4 (-2.37, -0.43)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Ghai, B. 2019	High	WOMAC Function	1 mos	PRP treatment	Normal saline: NS	Mean Difference	0.6 (-1.00, 2.20)	NS
Ghai, B. 2019	High	WOMAC Function	1.5 mos	PRP treatment	Normal saline: NS	Mean Difference	0.6 (-1.00, 2.20)	NS
Ghai, B. 2019	High	WOMAC Function	3 mos	PRP treatment	Normal saline: NS	Mean Difference	-3.9 (-6.81, -0.99)	PRP treatment
Ghai, B. 2019	High	WOMAC Function	6 mos	PRP treatment	Normal saline: NS	Mean Difference	-3.9 (-7.29, -0.51)	PRP treatment
Eroglu, 2016	Moderate	WOMAC Stiffness (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.19 (-1.38, 1.00)	NS
Eroglu, 2016	Moderate	WOMAC Stiffness	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	0 (-1.20, 1.20)	NS
Eroglu, 2016	Moderate	WOMAC Stiffness	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	0.15 (-0.92, 1.22)	NS
Eroglu, 2016	Moderate	WOMAC Function (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	0.7 (-5.63, 7.03)	NS
Eroglu, 2016	Moderate	WOMAC Function (WOMAC Physical (PA))	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.7 (-6.77, 5.37)	NS
Eroglu, 2016	Moderate	WOMAC Function (WOMAC Physical (PA))	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.63 (-6.82, 5.56)	NS
Elik, H. 2020	High	WOMAC Stiffness (WOMAC Scores)	1 mos	PRP treatment	Placebo	Mean Difference	-0.61 (-1.44, 0.22)	NS
Elik, H. 2020	High	WOMAC Stiffness (WOMAC Scores)	6 mos	PRP treatment	Placebo	Mean Difference	-1.62 (-2.54, -0.70)	PRP treatment
Elik, H. 2020	High	WOMAC Function (WOMAC Scores)	1 mos	PRP treatment	Placebo	Mean Difference	-5.27 (-12.12, 1.58)	NS
Elik, H. 2020	High	WOMAC Function (WOMAC Scores)	6 mos	PRP treatment	Placebo	Mean Difference	-11.99 (-19.08, -4.90)	PRP treatment
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	1 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	0 (-1.41, 1.41)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	2 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-1 (-2.41, 0.41)	NS
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	2 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-2 (-3.00, -1.00)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	3 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-2 (-3.41, -0.59)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	6 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-3 (-4.41, -1.59)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Stiffness (WOMAC Osteoarthritis Index Scores)	12 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-3 (-4.41, -1.59)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	1 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-3 (-9.40, 3.40)	NS
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	2 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-9 (-16.81, -1.19)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	2 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-13 (-22.90, -3.10)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	3 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-20 (-27.07, -12.93)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	6 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-23 (-31.49, -14.51)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Function (WOMAC Osteoarthritis Index Scores)	12 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-23 (-31.06, -14.94)	Intra-articular Autologous Conditioned Plasma Injections

Table 31: PICO 1h- 1: Platelet rich plasma vs. 1: Placebo- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Gormeli, 2017	High	EQ Pain	6 mos	PRP treatment: PRP injection 3 times (every 7 days)	Normal saline: 3 saline injections	Mean Difference	23.4 (19.65, 27.15)	PRP treatment
Gormeli, 2017	High	EQ Pain	6 mos	PRP treatment: PRP injection 1 time	Normal saline: 3 saline injections	Mean Difference	14 (11.56, 16.44)	PRP treatment
Wu, 2018	High	WOMAC Pain	2 wks	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-2.6 (-3.62, -1.58)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Pain	1 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-1.7 (-2.68, -0.72)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Pain	3 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-4.8 (-5.42, -4.18)	leukocyte and platelet-rich plasma
Wu, 2018	High	WOMAC Pain	6 mos	leukocyte and platelet-rich plasma: single 4ml inj. of PRP	Normal Saline: single 4-mL intra-articular injection	Mean Difference	-3.3 (-3.98, -2.62)	leukocyte and platelet-rich plasma
Patel. 2013	High	WOMAC Pain	6 wks	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Pain	3 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Pain	6 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Pain	6 wks	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Pain	3 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	WOMAC Pain	6 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Author Reported - analysis of variance (ANOVA)followed by post hoc tests	N/A	PRP
Patel. 2013	High	VAS Pain score	6 mos	PRP treatment: single 8ml inj. of PRP (1 mL of CaCl ₂ (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP); Total leucocyte count was zero	Normal Saline: Single 8ml inj. of normal saline	Mean Difference	-2.45 (-2.92, -1.98)	PRP treatment
Patel. 2013	High	VAS Pain score	6 mos	PRP treatment: two inj. of PRP 3 weeks apart	Normal Saline: Single 8ml inj. of normal saline	Mean Difference	-2.07 (-2.59, -1.55)	PRP treatment

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Ghai, B. 2019	High	VAS Pain score	1 mos	PRP treatment	Normal saline: NS	Mean Difference	-0.05 (-1.09, 0.99)	NS
Ghai, B. 2019	High	VAS Pain score	1.5 mos	PRP treatment	Normal saline: NS	Mean Difference	-1.2 (-2.46, 0.06)	NS
Ghai, B. 2019	High	VAS Pain score	3 mos	PRP treatment	Normal saline: NS	Mean Difference	-2.15 (-3.69, -0.61)	PRP treatment
Ghai, B. 2019	High	VAS Pain score	6 mos	PRP treatment	Normal saline: NS	Mean Difference	-0.85 (-3.22, 1.52)	NS
Ghai, B. 2019	High	WOMAC Pain	1 mos	PRP treatment	Normal saline: NS	Mean Difference	0.3 (-0.98, 1.58)	NS
Ghai, B. 2019	High	WOMAC Pain	1.5 mos	PRP treatment	Normal saline: NS	Mean Difference	0.25 (-0.96, 1.46)	NS
Ghai, B. 2019	High	WOMAC Pain	3 mos	PRP treatment	Normal saline: NS	Mean Difference	-3.45 (-5.83, -1.07)	PRP treatment
Ghai, B. 2019	High	WOMAC Pain	6 mos	PRP treatment	Normal saline: NS	Mean Difference	-3.05 (-5.79, -0.31)	PRP treatment
Qamar, 2021	High	VAS Pain score	1 mos	PRP injection: 3 weekly IA injections; double centrifuged PRP	IA Saline: 5 mL	Mean Difference	-4.4 (-15.33, 6.53)	NS
Qamar, 2021	High	VAS Pain score	3 mos	PRP injection: 3 weekly IA injections; double centrifuged PRP	IA Saline: 5 mL	Mean Difference	-13.46 (-21.44, -5.48)	PRP injection
Qamar, 2021	High	VAS Pain score	6 mos	PRP injection: 3 weekly IA injections; double centrifuged PRP	IA Saline: 5 mL	Mean Difference	-21.8 (-30.95, -12.65)	PRP injection
Eroglu, 2016	Moderate	WOMAC Pain (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.37 (-2.69, 1.95)	NS
Eroglu, 2016	Moderate	WOMAC Pain	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.69 (-2.93, 1.55)	NS
Eroglu, 2016	Moderate	WOMAC Pain	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Normal Saline: 0.09% NaCl 3 times with 3 weeks interval	Mean Difference	-0.52 (-2.58, 1.54)	NS
Elik, H. 2020	High	WOMAC Pain (WOMAC Scores)	1 mos	PRP treatment	Placebo	Mean Difference	-2.35 (-4.33, -0.37)	PRP treatment
Elik, H. 2020	High	WOMAC Pain (WOMAC Scores)	6 mos	PRP treatment	Placebo	Mean Difference	-4.01 (-6.03, -1.99)	PRP treatment
Smith, P. A. 2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	1 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-1 (-3.24, 1.24)	NS

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Smith, P. A.2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	2 wks	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-4 (-6.24, -1.76)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	2 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-4 (-6.83, -1.17)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	3 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-6 (-8.24, -3.76)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	6 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-6 (-8.24, -3.76)	Intra-articular Autologous Conditioned Plasma Injections
Smith, P. A.2016	High	WOMAC Pain (WOMAC Osteoarthritis Index Scores)	12 mos	Intra-articular Autologous Conditioned Plasma Injections	Placebo	Mean Difference	-7 (-9.83, -4.17)	Intra-articular Autologous Conditioned Plasma Injections

Table 32: PICO 1i- 1: Platelet rich plasma vs. 1: NSAID-

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Heredia, 2016	High	EURO QOL Pain Scale-Worsening	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RR	0.11(0.03,0.43)	Oral NSAID
Heredia, 2016	High	EURO QOL Pain Scale- Similar	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RR	1.44(0.76,2.74)	NS
Heredia, 2016	High	EURO QOL Pain Scale-Improvement	6 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RD	0.44(0.26,0.63)	Leukocyte-Poor Platelet Rich Plasma

Table 33: PICO 1i- 1: Platelet rich plasma vs. 1: NSAID- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Reyes-Sosa,2020	Moderate	WOMAC Total	12 mos	PRP treatment: 3 ml of activated PRP, re-inj. After 15 days	celecoxib: celecoxib 200 mg each 24 h for 1 year, irrespectively of the presence of pain	Author Reported - Kolmogorov–Smirnov and Shapiro–Wilk, two-tailed Fisher’s exact test, two-tailed Student’s t-test and Mann–Whitney U were performed when applicable	N/A	PRP Treatment

Table 34: PICO 1i- 1: Platelet rich plasma vs. 1: NSAID- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Ayeni, 2019	Moderate	WOMAC Function	2 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac (arthrotec) 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	WOMAC Function	3 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	WOMAC Function	4 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	WOMAC Function	5 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	PRP Treatment
Ayeni, 2019	Moderate	WOMAC Function	6 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Buendia-Lopez,2018	High	WOMAC Function, 20%Decrease	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RR	3.75(1.39,10.11)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Function, 20%Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RD	0.24(0.10,0.39)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness, 20%Decrease	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RR	3.75(1.39,10.11)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Stiffness, 20%Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RD	0.27(0.12,0.42)	Leukocyte-Poor Platelet Rich Plasma
Reyes-Sosa,2020	Moderate	WOMAC Function (WOMAC Physical (PA))	12 mos	PRP treatment: 3 ml of activated PRP, re-inj. After 15 days	celecoxib: celecoxib 200 mg each 24 h for 1 year, irrespectively of the presence of pain	Author Reported - Kolmogorov–Smirnov and Shapiro–Wilk, two-tailed Fisher’s exact test, two-tailed Student’s t-test and Mann–Whitney U were performed when applicable	N/A	PRP Treatment
Reyes-Sosa,2020	Moderate	WOMAC Stiffness	12 mos	PRP treatment: 3 ml of activated PRP, re-inj. After 15 days	celecoxib: celecoxib 200 mg each 24 h for 1 year, irrespectively of the presence of pain	Author Reported - Kolmogorov–Smirnov and Shapiro–Wilk, two-tailed Fisher’s exact test, two-tailed Student’s t-test and Mann–Whitney U were performed when applicable	N/A	PRP Treatment

Table 35: PICO 1i- 1: Platelet rich plasma vs. 1: NSAID- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Heredia, 2016	High	EUROQOL Pain Scale-Worsening	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RD	0.04(-0.03,0.11)	NS
Heredia, 2016	High	EUROQOL Pain Scale- Similar	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RR	0.96(0.57,1.64)	NS
Heredia, 2016	High	EUROQOL Pain Scale-Improvement	3 mos	Leukocyte-Poor Platelet Rich Plasma: 3 inj. 15 day interval	Oral NSAID: paracetamol and ibuprofen (metamizol/paracetamol) and anti-inflammatory drugs (ibuprofen 600 mg) with an alternate pattern of 575 mg metamizol/8 h and 1 g Paracetamol/8 h, together with 600 mg ibuprofen rescue if there were no contraindication such as hypertension)	RR	0.96(0.57,1.64)	NS
Ayeni, 2019	Moderate	VAS Pain score	2 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	VAS Pain score	3 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	VAS Pain score	4 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	VAS Pain score	5 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	NS
Ayeni, 2019	Moderate	VAS Pain score	6 mos	autologous PRP: 3 doses at 4 week intervals	Oral NSAID: oral diclofenac 75MG 12 hourly	Author Reported - analysis of variance (ANOVA)	N/A	PRP Treatment
Buendia-Lopez,2018	High	VAS Pain score	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	Mean Difference	-0.91 (-1.13, -0.69)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain, 20% Decrease	26 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RR	3.20(1.33,7.72)	Leukocyte-Poor Platelet Rich Plasma
Buendia-Lopez,2018	High	WOMAC Pain, 20% Decrease	52 wks	Leukocyte-Poor Platelet Rich Plasma: 5 mL Injection	Etoricoxib (Acoxel): 60 mg for 52 weeks	RD	0.30(0.15,0.46)	Leukocyte-Poor Platelet Rich Plasma

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Reyes-Sosa,2020	Moderate	WOMAC Pain	12 mos	PRP treatment: 3 ml of activated PRP, re-inj. After 15 days	celecoxib: celecoxib 200 mg each 24 h for 1 year, irrespectively of the presence of pain	Author Reported - Kolmogorov-Smirnov and Shapiro-Wilk, two-tailed Fisher's exact test, two-tailed Student's t-test and Mann-Whitney U were performed when applicable	N/A	PRP Treatment
Reyes-Sosa,2020	Moderate	VAS Pain score	12 mos	PRP treatment: 3 ml of activated PRP, re-inj. After 15 days	celecoxib: celecoxib 200 mg each 24 h for 1 year, irrespectively of the presence of pain	Author Reported - Kolmogorov-Smirnov and Shapiro-Wilk, two-tailed Fisher's exact test, two-tailed Student's t-test and Mann-Whitney U were performed when applicable	N/A	PRP Treatment

Table 36: PICO 1j- 1: Platelet rich plasma vs. 1: Ozone- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Duymus, 2017	Moderate	WOMAC Total	1 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-4.7 (-10.06, 0.66)	NS
Duymus, 2017	Moderate	WOMAC Total	3 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-20.9 (-26.80, -15.00)	PRP treatment
Duymus, 2017	Moderate	WOMAC Total	6 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-33.8 (-38.09, -29.51)	PRP treatment
Duymus, 2017	Moderate	WOMAC Total	12 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-22.1 (-27.08, -17.12)	PRP treatment
Raeissadat, 2021	High	WOMAC Total	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	5.9 (3.54, 8.26)	Ozone Injection
Raeissadat, 2021	High	WOMAC Total	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-7.1 (-9.46, -4.74)	PRP injection
Raeissadat, 2021	High	WOMAC Total	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-9.1 (-11.46, -6.74)	PRP injection
Raeissadat, 2021	High	LEQ Total	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	1.3 (0.58, 2.02)	Ozone Injection
Raeissadat, 2021	High	LEQ Total	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-1.6 (-2.32, -0.88)	PRP injection
Raeissadat, 2021	High	LEQ Total	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-1.9 (-2.54, -1.26)	PRP injection
Raeissadat, 2021	High	WOMAC Total	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	5.6 (2.99, 8.21)	Ozone Injection
Raeissadat, 2021	High	WOMAC Total	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-7.5 (-10.19, -4.81)	PRGF
Raeissadat, 2021	High	WOMAC Total	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-9.5 (-12.19, -6.81)	PRGF
Raeissadat, 2021	High	LEQ Total	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	1.5 (0.78, 2.22)	Ozone Injection
Raeissadat, 2021	High	LEQ Total	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-1.5 (-2.22, -0.78)	PRGF
Raeissadat, 2021	High	LEQ Total	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-1.7 (-2.51, -0.89)	PRGF

Table 37: PICO 1j- 1: Platelet rich plasma vs. 1: Ozone- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Gaballa, 2019	Moderate	WOMAC Function	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	-12.9 (-17.55, -8.25)	PRP treatment
Gaballa, 2019	Moderate	WOMAC Function	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	-23.1 (-28.03, -18.17)	PRP treatment
Gaballa, 2019	Moderate	6 min walk	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	25.7 (-7.61, 59.01)	NS
Gaballa, 2019	Moderate	6 min walk	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	41 (0.13, 81.87)	PRP treatment
Duymus, 2017	Moderate	WOMAC Stiffness	1 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	0.1 (-0.50, 0.70)	NS
Duymus, 2017	Moderate	WOMAC Stiffness	3 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-1.2 (-1.77, -0.63)	PRP treatment
Duymus, 2017	Moderate	WOMAC Stiffness	6 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-2.8 (-3.21, -2.39)	PRP treatment
Duymus, 2017	Moderate	WOMAC Stiffness	12 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-1.8 (-2.21, -1.39)	PRP treatment
Duymus, 2017	Moderate	WOMAC Function	1 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-2 (-5.74, 1.74)	NS
Duymus, 2017	Moderate	WOMAC Function	3 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-365 (-369.44, -360.56)	PRP treatment
Duymus, 2017	Moderate	WOMAC Function	6 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-24.5 (-27.60, -21.40)	PRP treatment
Duymus, 2017	Moderate	WOMAC Function	12 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-15.6 (-19.31, -11.89)	PRP treatment
Raeissadat, 2021	High	WOMAC Stiffness	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.1 (-0.46, 0.26)	NS
Raeissadat, 2021	High	WOMAC Stiffness	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.7 (-1.12, -0.28)	PRP injection
Raeissadat, 2021	High	WOMAC Stiffness	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.8 (-1.14, -0.46)	PRP injection
Raeissadat, 2021	High	WOMAC Function	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	4.8 (2.94, 6.66)	Ozone Injection
Raeissadat, 2021	High	WOMAC Function	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-4.6 (-6.52, -2.68)	PRP injection
Raeissadat, 2021	High	WOMAC Function	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-5.6 (-7.23, -3.97)	PRP injection

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2021	High	LEQ Walking	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.16 (-0.35, 0.03)	NS
Raeissadat, 2021	High	LEQ Walking	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.16 (-0.32, -0.00)	PRP injection
Raeissadat, 2021	High	LEQ Walking	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.19 (-0.41, 0.03)	NS
Raeissadat, 2021	High	LEQ ADL	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	0 (-0.32, 0.32)	NS
Raeissadat, 2021	High	LEQ ADL	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.8 (-1.16, -0.44)	PRP injection
Raeissadat, 2021	High	LEQ ADL	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.7 (-1.02, -0.38)	PRP injection
Raeissadat, 2021	High	WOMAC Stiffness	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.1 (-0.57, 0.37)	NS
Raeissadat, 2021	High	WOMAC Stiffness	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.7 (-1.28, -0.12)	PRGF
Raeissadat, 2021	High	WOMAC Stiffness	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.76 (-1.16, -0.36)	PRGF
Raeissadat, 2021	High	WOMAC Function	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	4.5 (2.48, 6.52)	Ozone Injection
Raeissadat, 2021	High	WOMAC Function	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-5.1 (-7.18, -3.02)	PRGF
Raeissadat, 2021	High	WOMAC Function	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-6.1 (-8.12, -4.08)	PRGF
Raeissadat, 2021	High	LEQ Walking	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.1 (-0.32, 0.12)	NS
Raeissadat, 2021	High	LEQ Walking	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.16 (-0.32, -0.00)	PRGF
Raeissadat, 2021	High	LEQ Walking	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.14 (-0.38, 0.10)	NS
Raeissadat, 2021	High	LEQ ADL	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	0.1 (-0.22, 0.42)	NS
Raeissadat, 2021	High	LEQ ADL	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.8 (-1.16, -0.44)	PRGF
Raeissadat, 2021	High	LEQ ADL	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.7 (-1.02, -0.38)	PRGF

Table 38: PICO 1j- 1: Platelet rich plasma vs. 1: Ozone- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Gaballa, 2019	Moderate	VAS Pain score	1 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	-1.1 (-1.92, -0.28)	PRP treatment
Gaballa, 2019	Moderate	VAS Pain score	3 mos	PRP treatment: 2 inj. (one every 2 wk)	Ozone therapy: weekly intra-articular ozone injection for 4 successive weeks	Mean Difference	-2.6 (-3.52, -1.68)	PRP treatment
Duymus, 2017	Moderate	VAS Pain score	1 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-1 (-1.55, -0.45)	PRP treatment
Duymus, 2017	Moderate	VAS Pain score	3 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-2.8 (-3.26, -2.34)	PRP treatment
Duymus, 2017	Moderate	VAS Pain score	6 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-3.3 (-3.86, -2.74)	PRP treatment
Duymus, 2017	Moderate	VAS Pain score	12 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-2.5 (-3.07, -1.93)	PRP treatment
Duymus, 2017	Moderate	WOMAC Pain	1 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	0.2 (-1.11, 1.51)	NS
Duymus, 2017	Moderate	WOMAC Pain	3 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-3.86 (-5.25, -2.47)	PRP treatment
Duymus, 2017	Moderate	WOMAC Pain	6 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-6.6 (-7.72, -5.48)	PRP treatment
Duymus, 2017	Moderate	WOMAC Pain	12 mos	PRP treatment: 2 injections per month	Ozone therapy: 4 Injections/ week	Mean Difference	-4.8 (-6.04, -3.56)	PRP treatment
Raeissadat, 2021	High	WOMAC Pain	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	1.1 (0.46, 1.74)	Ozone Injection
Raeissadat, 2021	High	WOMAC Pain	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-1.7 (-2.41, -0.99)	PRP injection
Raeissadat, 2021	High	WOMAC Pain	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-2.7 (-3.27, -2.13)	PRP injection
Raeissadat, 2021	High	LEQ Pain	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	1.2 (0.78, 1.62)	Ozone Injection
Raeissadat, 2021	High	LEQ Pain	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.4 (-0.76, -0.04)	PRP injection
Raeissadat, 2021	High	LEQ Pain	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.9 (-1.32, -0.48)	PRP injection
Raeissadat, 2021	High	VAS Pain score	2 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	0.7 (0.20, 1.20)	Ozone Injection
Raeissadat, 2021	High	VAS Pain score	6 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-0.6 (-1.10, -0.10)	PRP injection

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Raeissadat, 2021	High	VAS Pain score	12 mos	PRP injection: 2 doses/3 weeks	Ozone Injection: 3 doses weekly	Mean Difference	-2 (-2.50, -1.50)	PRP injection
Raeissadat, 2021	High	WOMAC Pain	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	1.1 (0.38, 1.82)	Ozone Injection
Raeissadat, 2021	High	WOMAC Pain	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-1.7 (-2.48, -0.92)	PRGF
Raeissadat, 2021	High	WOMAC Pain	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-2.7 (-3.42, -1.98)	PRGF
Raeissadat, 2021	High	LEQ Pain	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	1.2 (0.70, 1.70)	Ozone Injection
Raeissadat, 2021	High	LEQ Pain	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.4 (-0.85, 0.05)	NS
Raeissadat, 2021	High	LEQ Pain	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.8 (-1.22, -0.38)	PRGF
Raeissadat, 2021	High	VAS Pain score	2 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	0.7 (0.20, 1.20)	Ozone Injection
Raeissadat, 2021	High	VAS Pain score	6 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-0.5 (-1.00, 0.00)	NS
Raeissadat, 2021	High	VAS Pain score	12 mos	PRGF: 2 doses with 3 wk intervals	Ozone Injection: 3 doses weekly	Mean Difference	-2.1 (-2.60, -1.60)	PRGF

Table 39: PICO 1I- 1: Platelet rich plasma vs. 1: Prolotherapy- Composite

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rahimzadeh,2018	High	WOMAC Total	1 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-0.9 (-6.72, 4.92)	NS
Rahimzadeh,2018	High	WOMAC Total	2 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-7.7 (-12.58, -2.82)	PRP treatment
Rahimzadeh,2018	High	WOMAC Total	6 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-7.3 (-12.50, -2.10)	PRP treatment
Eroglu, 2016	Moderate	WOMAC Total (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.45 (-8.51, 9.41)	NS
Eroglu, 2016	Moderate	WOMAC Total	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.61 (-7.44, 8.66)	NS
Eroglu, 2016	Moderate	WOMAC Total	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.46 (-7.36, 8.28)	NS

Table 40: PICO 1I- 1: Platelet rich plasma vs. 1: Prolotherapy- Function

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rahimzadeh,2018	High	WOMAC Function (WOMAC Physical (PA))	1 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-0.7 (-4.92, 3.52)	NS
Rahimzadeh,2018	High	WOMAC Function (WOMAC Physical (PA))	2 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-5.4 (-9.28, -1.52)	PRP treatment
Rahimzadeh,2018	High	WOMAC Function (WOMAC Physical (PA))	6 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-5 (-9.05, -0.95)	PRP treatment
Rahimzadeh,2018	High	WOMAC Stiffness	1 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	0.1 (-0.57, 0.77)	NS
Rahimzadeh,2018	High	WOMAC Stiffness	2 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-0.5 (-0.92, -0.08)	PRP treatment
Rahimzadeh,2018	High	WOMAC Stiffness	6 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-0.5 (-0.95, -0.05)	PRP treatment
Eroglu, 2016	Moderate	WOMAC Stiffness (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	-0.04 (-1.11, 1.03)	NS
Eroglu, 2016	Moderate	WOMAC Stiffness	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.2 (-0.86, 1.26)	NS
Eroglu, 2016	Moderate	WOMAC Stiffness	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	-0.3 (-1.11, 0.51)	NS
Eroglu, 2016	Moderate	WOMAC Function (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.3 (-6.28, 6.88)	NS
Eroglu, 2016	Moderate	WOMAC Function (WOMAC Physical (PA))	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.1 (-5.83, 6.03)	NS
Eroglu, 2016	Moderate	WOMAC Function (WOMAC Physical (PA))	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	-0.28 (-6.23, 5.67)	NS

Table 41: PICO 1I- 1: Platelet rich plasma vs. 1: Prolotherapy- Pain

Reference Title	Quality	Outcome Details	Duration	Treatment 1 (Details)	Treatment 2 (Details)	Effect Measure	Result (95% CI)	Favored Treatment
Rahimzadeh,2018	High	WOMAC Pain	1 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-0.3 (-1.82, 1.22)	NS
Rahimzadeh,2018	High	WOMAC Pain	2 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-1.7 (-2.76, -0.64)	PRP treatment
Rahimzadeh,2018	High	WOMAC Pain	6 mos	PRP treatment: 7 mL PRP solution	Prolotherapy: 7 mL 25% dextrose	Mean Difference	-1.8 (-2.93, -0.67)	PRP treatment
Eroglu, 2016	Moderate	WOMAC Pain (Before 2 nd injection)	Postop.	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.18 (-2.10, 2.46)	NS
Eroglu, 2016	Moderate	WOMAC Pain	3 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	0.31 (-1.76, 2.38)	NS
Eroglu, 2016	Moderate	WOMAC Pain	6 mos	PRP treatment: 3 times with 3 weeks intervals. Before the injection, the PRP was activated by adding 10% calcium chloride.	Prolotherapy: dextrose prolotherapy 3 times with 3 wks interval	Mean Difference	1.03 (-0.78, 2.84)	NS

Quality Appraisal

All studies which are considered for inclusion are evaluated using a standardized quality appraisal form and scoring key. In the quality evaluation report, domains with no flaws or a low risk of bias will be represented as a full black circle ●. Domains with a high risk of bias will be represented as a circle with a white center ○, and domains which are uncertain or not clearly stated in the study's methodology will be represented as a half black/half white circle ◐.

Randomized Study Appraisal Form

Resources used to develop the Randomized Trial Quality Appraisal System:

- GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004; (328): 1490-1494.
- Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org. The following domains are evaluated to determine the study quality of randomized study designs.
- Guyatt, G. H., Oxman, A. D., Sultan, S., et al. (2011). GRADE guidelines: 9. Rating up the quality of evidence. *Journal of Clinical Epidemiology*, 64(12), 1311–1316.

The following domains are evaluated to determine the study quality of randomized study designs.

- Random Sequence Generation
- Allocation Concealment
- Blinding of Participants and Personnel
- Incomplete Outcome Data
- Selective Reporting
- Other Bias

Randomized Study Design Quality Key:

High Quality Study	<2 Flaw
Moderate Quality Study	≥2 and <4 Flaws
Low Quality Study	≥4 and <6 Flaws
Very Low Quality Study	≥6 Flaws

Intervention - Randomized

Study	Random Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias	Inclusion	Strength
Ahmad, H. S., 2018	●	●	●	●	●	●	Include	High Quality
Akan, A., 2018	●	●	○	●	●	●	Include	High Quality
Angoorani, H., 2015	●	●	○	●	●	●	Include	High Quality
Anz, A. W., 2020	●	●	○	●	●	●	Include	Moderate Quality
Bansal, H., 2021	●	●	●	●	●	●	Include	High Quality
Basnaev, U. I., 2021	●	●	○	●	●	●	Include	Moderate Quality
Buendia-Lopez, D., 2018	●	●	●	●	●	●	Include	High Quality
Cerza, F., 2012	○	●	○	●	●	●	Include	Moderate Quality
Cole, B. J., 2017	●	●	●	●	●	●	Include	High Quality
Di Martino, A., 2019	●	●	●	●	●	●	Include	High Quality
Duymus, T. M., 2017	●	●	○	●	●	○	Include	Moderate Quality
Elawamy, A., 2021	●	●	○	●	●	●	Include	Moderate Quality
Elgendy, M. H., 2020	●	●	○	●	●	●	Include	High Quality
Elik, H., 2020	●	●	●	●	●	●	Include	High Quality
Elksnins-Finogejevs, A., 2020	●	●	○	●	●	●	Include	High Quality
EROGLU, Ali, 2016	●	●	○	●	●	●	Include	Moderate Quality
Forogh, B., 2016	●	●	●	●	●	●	Include	High Quality
Gaballa, N. M., 2019	●	○	○	●	●	●	Include	Moderate Quality
Ghai, B., 2019	●	●	●	●	●	●	Include	High Quality
Gormeli, G., 2017	●	●	●	●	●	●	Include	High Quality
Huang, Y., 2019	●	●	○	●	●	●	Include	Moderate Quality
Joshi Jubert, N., 2017	●	●	●	●	●	●	Include	High Quality
Khan, A. F., 2018	●	●	●	●	●	●	Include	High Quality
Lin, K. Y., 2019	●	●	●	●	●	●	Include	High Quality
Lisi, C., 2018	●	●	●	●	●	●	Include	High Quality
Louis, M. L., 2018	●	●	●	○	●	●	Include	High Quality
Louis, M. L., 2021	●	●	●	●	●	●	Include	High Quality
Montanez-Heredia, E., 2016	●	●	●	●	●	●	Include	High Quality
Nabi, B. N., 2018	●	○	●	●	●	●	Include	High Quality
Park, Y. B., 2021	●	●	●	●	●	●	Include	High Quality
Patel, S., 2013	●	●	●	●	●	●	Include	High Quality

Study	Random Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias	Inclusion	Strength
Phul, S. H., 2018	●	●	●	●	●	○	Include	Moderate Quality
Pishgahi, A., 2020	●	○	○	●	●	●	Include	Moderate Quality
Qamar, A., 2021	●	●	●	●	●	●	Include	High Quality
Raeissadat, S. A., 2015	●	●	○	●	●	●	Include	High Quality
Raeissadat, S. A., 2017	●	○	○	●	●	●	Include	Moderate Quality
Raeissadat, S. A., 2020	●	●	●	●	●	●	Include	High Quality
Raeissadat, S. A., 2020	●	●	●	●	●	●	Include	High Quality
Raeissadat, S. A., 2021	●	●	●	●	●	●	Include	High Quality
Rahimzadeh, P., 2018	●	●	●	●	●	●	Include	High Quality
Rayegani, S. M., 2014	●	●	○	●	●	●	Include	High Quality
Reyes-Sosa, R., 2020	●	●	○	●	●	●	Include	Moderate Quality
Sánchez, M., 2012	●	●	●	●	●	●	Include	High Quality
Simental-Mendia, M., 2016	●	●	○	●	●	●	Include	Moderate Quality
Smith, P. A., 2016	●	●	●	●	●	●	Include	High Quality
Spakova, T., 2012	●	●	○	●	●	●	Include	Moderate Quality
Su, K., 2018	●	○	○	●	●	●	Include	Moderate Quality
Tavassoli, M., 2019	●	●	○	●	●	●	Include	High Quality
Uslu Guvendi, E., 2018	●	●	○	●	●	●	Include	High Quality
Vaquerizo, V., 2013	●	●	●	●	●	●	Include	High Quality
Wu, Y. T., 2018	●	●	●	●	●	●	Include	High Quality
Xu, Z., 2021	●	●	●	○	●	●	Include	High Quality

Included Articles

1. Ahmad, H. S., Farrag, S. E., Okasha, A. E., Kadry, A. O., Ata, T. B., Monir, A. A., Shady, I. Clinical outcomes are associated with changes in ultrasonographic structural appearance after platelet-rich plasma treatment for knee osteoarthritis. *International Journal of Rheumatic Diseases* 2018; 5: 960-966
2. Akan, Ö, Sarikaya, N. Ö, Koçyigit, H. Efficacy of platelet-rich plasma administration in patients with severe knee osteoarthritis: Can platelet-rich plasma administration delay arthroplasty in this patient population?. *International journal of clinical and experimental medicine* 2018; 9: 9473-9483
3. Angoorani, H., Mazaherinezhad, A., Marjomaki, O., Younespour, S. Treatment of knee osteoarthritis with platelet-rich plasma in comparison with transcutaneous electrical nerve stimulation plus exercise: a randomized clinical trial. *Medical Journal of the Islamic Republic of Iran* 2015; 0: 223
4. Anz, A. W., Hubbard, R., Rendos, N. K., Everts, P. A., Andrews, J. R., Hackel, J. G. Bone Marrow Aspirate Concentrate Is Equivalent to Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis at 1 Year: A Prospective, Randomized Trial. *Orthopaedic Journal of Sports Medicine* 2020; 2: 2325967119900958
5. Ayeni, F., Esan, O., Ikem, I. C., Adegbehingbe, O. Early outcome of platelet rich plasma and non-steroidal anti-inflammatory agent alone and in combination on primary knee osteoarthritis. *Journal of Clinical and Diagnostic Research* 2019; 11: RC06-RC08
6. Bansal, H., Leon, J., Pont, J. L., Wilson, D. A., Bansal, A., Agarwal, D., Preoteasa, I. Platelet-rich plasma (PRP) in osteoarthritis (OA) knee: Correct dose critical for long term clinical efficacy. *Scientific Reports* 2021; 1: 3971
7. Basnaev, U. I., Karakursakov, N. E., Mykhaylichenko, V. Y., Kriventsov, M. A. Platelet-rich plasma administering in osteoarthrosis treatment. *Russian Open Medical Journal* 2021; 1:
8. Buendia-Lopez, D., Medina-Quiros, M., Fernandez-Villacanas Marin, M. A. Clinical and radiographic comparison of a single LP-PRP injection, a single hyaluronic acid injection and daily NSAID administration with a 52-week follow-up: a randomized controlled trial. *Journal of Orthopaedics & Traumatology* 2018; 1: 3
9. Cerza, F., Carni, S., Carcangiu, A., Di Vavo, I., Schiavilla, V., Pecora, A., De Biasi, G., Ciuffreda, M. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. *American Journal of Sports Medicine* 2012; 12: 2822-7
10. Cole, B. J., Karas, V., Hussey, K., Pilz, K., Fortier, L. A. Hyaluronic Acid Versus Platelet-Rich Plasma: A Prospective, Double-Blind Randomized Controlled Trial Comparing Clinical Outcomes and Effects on Intra-articular Biology for the Treatment of Knee Osteoarthritis. *American Journal of Sports Medicine* 2017; 2: 339-346
11. Di Martino, A., Di Matteo, B., Papio, T., Tentoni, F., Selleri, F., Cenacchi, A., Kon, E., Filardo, G. Platelet-Rich Plasma Versus Hyaluronic Acid Injections for the Treatment of Knee

- Osteoarthritis: Results at 5 Years of a Double-Blind, Randomized Controlled Trial. *American Journal of Sports Medicine* 2019; 2: 347-354
12. Duymus, T. M., Mutlu, S., Dernek, B., Komur, B., Aydogmus, S., Kesiktas, F. N. Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017; 2: 485-492
 13. Elawamy, A., Kamel, E. Z., Mahran, S. A., Abdellatif, H., Hassanien, M. Efficacy of Genicular Nerve Radiofrequency Ablation Versus Intra-Articular Platelet Rich Plasma in Chronic Knee Osteoarthritis: A Single-Blind Randomized Clinical Trial. *Pain Physician* 2021; 2: 127-134
 14. Elgendy, M. H., Elsamahy, S. A., Mostafa, M. S. E. M., Hamza, M. S. K. Efficacy of shockwave therapy versus intra-articular platelet-rich plasma injection in management of knee osteoarthritis: A randomized controlled trial. *International Journal of Pharmaceutical Research* 2020; 4: 4283-4289
 15. Elik, H., Dogu, B., Yilmaz, F., Begoglu, F. A., Kuran, B. The efficiency of platelet-rich plasma treatment in patients with knee osteoarthritis. *Journal of Back & Musculoskeletal Rehabilitation* 2020; 1: 127-138
 16. Elksnins-Finogejevs, A., Vidal, L., Peredistijs, A. Intra-articular platelet-rich plasma vs corticosteroids in the treatment of moderate knee osteoarthritis: a single-center prospective randomized controlled study with a 1-year follow up. *Journal of Orthopaedic Surgery* 2020; 1: 257
 17. EROGLU, Ali, Aylin, SARI, DURMUS, Bekir Platelet-rich plasma vs prolotherapy in the management of knee osteoarthritis: randomized placebo-controlled trial. *Spor Hekimligi Dergisi* 2016; 2: 034-043
 18. Forogh, B., Mianehsaz, E., Shoaee, S., Ahadi, T., Raissi, G. R., Sajadi, S. Effect of single injection of platelet-rich plasma in comparison with corticosteroid on knee osteoarthritis: a double-blind randomized clinical trial. *Journal of Sports Medicine & Physical Fitness* 2016; 7: 901-8
 19. Gaballa, N. M., Mohammed, Y. A., Kamel, L. M., Mahgoub, H. M. Therapeutic efficacy of intra-articular injection of platelet-rich plasma and ozone therapy in patients with primary knee osteoarthritis. *Egyptian Rheumatologist* 2019; 3: 183-187
 20. Ghai, B., Gupta, V., Jain, A., Goel, N., Chouhan, D., Batra, Y. K. Effectiveness of platelet rich plasma in pain management of osteoarthritis knee: double blind, randomized comparative study. *Brazilian Journal of Anesthesiology* 2019; 5: 439-447
 21. Gormeli, G., Gormeli, C. A., Ataoglu, B., Colak, C., Aslanturk, O., Ertem, K. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy* 2017; 3: 958-965
 22. Huang, Y., Liu, X., Xu, X., Liu, J. Intra-articular injections of platelet-rich plasma, hyaluronic acid or corticosteroids for knee osteoarthritis : A prospective randomized controlled study. *Orthopade* 2019; 3: 239-247

23. Joshi Jubert, N., Rodriguez, L., Reverte-Vinaixa, M. M., Navarro, A. Platelet-Rich Plasma Injections for Advanced Knee Osteoarthritis: A Prospective, Randomized, Double-Blinded Clinical Trial. *Orthopaedic Journal of Sports Medicine* 2017; 2: 2325967116689386
24. Khan, A. F., Gillani, S. F. U. H. S., Khan, A. F. Role of intra-articular corticosteroid with xylocaine vs plate rich plasma for the treatment of early grade II knee osteoarthritis at Akhtar Saeed Teaching Hospital Lahore: A randomized controlled trail. *Pakistan Journal of Medical and Health Sciences* 2018; 4: 1432-1435
25. Lana, J. F., Weglein, A., Sampson, S. E., Vicente, E. F., Huber, S. C., Souza, C. V., Ambach, M. A., Vincent, H., Urban-Paffaro, A., Onodera, C. M., Annichino-Bizzacchi, J. M., Santana, M. H., Belangero, W. D. Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee. *Journal of Stem Cells & Regenerative Medicine* 2016; 2: 69-78
26. Lin, K. Y., Yang, C. C., Hsu, C. J., Yeh, M. L., Renn, J. H. Intra-articular Injection of Platelet-Rich Plasma Is Superior to Hyaluronic Acid or Saline Solution in the Treatment of Mild to Moderate Knee Osteoarthritis: A Randomized, Double-Blind, Triple-Parallel, Placebo-Controlled Clinical Trial. *Arthroscopy* 2019; 1: 106-117
27. Lisi, C., Perotti, C., Scudeller, L., Sammarchi, L., Dametti, F., Musella, V., Di Natali, G. Treatment of knee osteoarthritis: platelet-derived growth factors vs. hyaluronic acid. A randomized controlled trial. *Clinical Rehabilitation* 2018; 3: 330-339
28. Louis, M. L., Magalon, J., Jouve, E., Bornet, C. E., Mattei, J. C., Chagnaud, C., Rochwerger, A., Veran, J., Sabatier, F. Growth Factors Levels Determine Efficacy of Platelets Rich Plasma Injection in Knee Osteoarthritis: A Randomized Double Blind Noninferiority Trial Compared With Viscosupplementation. *Arthroscopy* 2018; 5: 1530-1540.e2
29. Montanez-Heredia, E., Irizar, S., Huertas, P. J., Otero, E., Del Valle, M., Prat, I., Diaz-Gallardo, M. S., Peran, M., Marchal, J. A., Hernandez-Lamas Mdel, C. Intra-Articular Injections of Platelet-Rich Plasma versus Hyaluronic Acid in the Treatment of Osteoarthritic Knee Pain: A Randomized Clinical Trial in the Context of the Spanish National Health Care System. *International Journal of Molecular Sciences* 2016; 7: 02
30. Nabi, B. N., Sedighinejad, A., Mardani-Kivi, M., Haghghi, M., Roushan, Z. A., Tehran, S. G., Biazar, G. Comparing the effectiveness of intra-articular platelet-rich plasma and corticosteroid injection under ultrasound guidance on pain control of knee osteoarthritis. *Iranian Red Crescent Medical Journal* 2018; 3:
31. Park, Y. B., Kim, J. H., Ha, C. W., Lee, D. H. Clinical Efficacy of Platelet-Rich Plasma Injection and Its Association With Growth Factors in the Treatment of Mild to Moderate Knee Osteoarthritis: A Randomized Double-Blind Controlled Clinical Trial As Compared With Hyaluronic Acid. *American Journal of Sports Medicine* 2021; 2: 487-496
32. Patel, S., Dhillon, M. S., Aggarwal, S., Marwaha, N., Jain, A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *American Journal of Sports Medicine* 2013; 2: 356-64
33. Phul, S. H., Mobushir, M., Jilani, R. U. A., Khan, I. S., Malik, H., Jan, G. Comparison of intra-articular steroids injection versus platelets rich plasma injection in patients with osteoarthritic knee joints. *Pakistan Journal of Medical and Health Sciences* 2018; 3: 931-934

34. Pishgahi, A., Abolhasan, R., Shakouri, S. K., Soltani-Zangbar, M. S., Dareshiri, S., Ranjbar Kiyakalayeh, S., Khoeilar, A., Zamani, M., Motavalli Khiavi, F., Pourabbas Kheiraddin, B., Mehdizadeh, A., Yousefi, M. Effect of Dextrose Prolotherapy, Platelet Rich Plasma and Autologous Conditioned Serum on Knee Osteoarthritis: A Randomized Clinical Trial. *Iranian Journal of Allergy Asthma & Immunology* 2020; 3: 243-252
35. Qamar, A., Mohsin, S. N., Siddiqui, U. N., Naz, S., Danish, S. Effectiveness of platelet rich plasma for the management of knee osteoarthritis: A randomized placebo controlled trial. *Pakistan Journal of Medical and Health Sciences* 2021; 7: 1553-1556
36. Raeissadat, S. A., Ahangar, A. G., Rayegani, S. M., Sajjadi, M. M., Ebrahimpour, A., Yavari, P. Platelet-rich plasma-derived growth factor vs hyaluronic acid injection in the individuals with knee osteoarthritis: A one year randomized clinical trial. *Journal of pain research* 2020; 0: 1699-1711
37. Raeissadat, S. A., Ghazi Hosseini, P., Bahrami, M. H., Salman Roghani, R., Fathi, M., Gharooee Ahangar, A., Darvish, M. The comparison effects of intra-articular injection of Platelet Rich Plasma (PRP), Plasma Rich in Growth Factor (PRGF), Hyaluronic Acid (HA), and ozone in knee osteoarthritis; a one year randomized clinical trial. *BMC Musculoskeletal Disorders* 2021; 1: 134
38. Raeissadat, S. A., Ghorbani, E., Taheri, M. S., Soleimani, R., Rayegani, S. M., Babae, M., Payami, S. MRI changes after platelet rich plasma injection in knee osteoarthritis (Randomized clinical trial). *Journal of pain research* 2020; 0: 65-73
39. Raeissadat, S. A., Rayegani, S. M., Ahangar, A. G., Abadi, P. H., Mojjani, P., Ahangar, O. G. Efficacy of Intra-articular Injection of a Newly Developed Plasma Rich in Growth Factor (PRGF) Versus Hyaluronic Acid on Pain and Function of Patients with Knee Osteoarthritis: A Single-Blinded Randomized Clinical Trial. *Clinical medicine insights. Arthritis and musculoskeletal disorders* 2017; 0: 1179544117733452
40. Raeissadat, S. A., Rayegani, S. M., Hassanabadi, H., Fathi, M., Ghorbani, E., Babae, M., Azma, K. Knee Osteoarthritis Injection Choices: Platelet- Rich Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial). *Clinical medicine insights. Arthritis and musculoskeletal disorders* 2015; 0: 1-8
41. Rahimzadeh, P., Imani, F., Faiz, S. H. R., Entezary, S. R., Zamanabadi, M. N., Alebouyeh, M. R. The effects of injecting intra-articular platelet-rich plasma or prolotherapy on pain score and function in knee osteoarthritis. *Clinical Interventions In Aging* 2018; 0: 73-79
42. Rayegani, S. M., Raeissadat, S. A., Taheri, M. S., Babae, M., Bahrami, M. H., Eliaspour, D., Ghorbani, E. Does intra articular platelet rich plasma injection improve function, pain and quality of life in patients with osteoarthritis of the knee? A randomized clinical trial. *Orthopedic Reviews* 2014; 3: 5405
43. Reyes-Sosa, R., Lugo-Radillo, A., Ruiz-Olivera, M. R., Cruz-Santiago, L., García-Cruz, C. R., Mendoza-Cano, O. Clinical comparison of platelet-rich plasma injection and daily celecoxib administration in the treatment of early knee osteoarthritis: A randomized clinical trial. *Journal of Applied Biomedicine* 2020; 2: 41-45
44. Sánchez, M., Fiz, N., Azofra, J., Usabiaga, J., Aduriz Recalde, E., Garcia Gutierrez, A., Albillos, J., Gárate, R., Aguirre, J. J., Padilla, S., Orive, G., Anitua, E. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy* 2012; 8: 1070-8

45. Simental-Mendia, M., Vilchez-Cavazos, J. F., Pena-Martinez, V. M., Said-Fernandez, S., Lara-Arias, J., Martinez-Rodriguez, H. G. Leukocyte-poor platelet-rich plasma is more effective than the conventional therapy with acetaminophen for the treatment of early knee osteoarthritis. *Archives of Orthopaedic & Trauma Surgery* 2016; 12: 1723-1732
46. Smith, P. A. Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis: An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial. *American Journal of Sports Medicine* 2016; 4: 884-91
47. Spakova, T., Rosocha, J., Lacko, M., Harvanova, D., Gharaibeh, A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. *American Journal of Physical Medicine & Rehabilitation* 2012; 5: 411-7
48. Su, K., Bai, Y., Wang, J., Zhang, H., Liu, H., Ma, S. Comparison of hyaluronic acid and PRP intra-articular injection with combined intra-articular and intraosseous PRP injections to treat patients with knee osteoarthritis. *Clinical Rheumatology* 2018; 5: 1341-1350
49. Tavassoli, M., Janmohammadi, N., Hosseini, A., Khafri, S., Esmailnejad-Ganji, S. M. Single- and double-dose of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: A randomized controlled trial. *World Journal of Orthopedics* 2019; 9: 310-326
50. Uslu Guvendi, E., Askin, A., Guvendi, G., Kocyigit, H. Comparison of Efficiency Between Corticosteroid and Platelet Rich Plasma Injection Therapies in Patients With Knee Osteoarthritis. *Archives of Rheumatology* 2018; 3: 273-281
51. Vaquerizo, V., Plasencia, M^Á, Arribas, I., Seijas, R., Padilla, S., Orive, G., Anitua, E. Comparison of intra-articular injections of plasma rich in growth factors (PRGF-Endoret) versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trial. *Arthroscopy* 2013; 10: 1635-43
52. Wu, Y. T., Hsu, K. C., Li, T. Y., Chang, C. K., Chen, L. C. Effects of Platelet-Rich Plasma on Pain and Muscle Strength in Patients With Knee Osteoarthritis. *American Journal of Physical Medicine & Rehabilitation* 2018; 4: 248-254
53. Xu, Z., He, Z., Shu, L., Li, X., Ma, M., Ye, C. Intra-Articular Platelet-Rich Plasma Combined With Hyaluronic Acid Injection for Knee Osteoarthritis Is Superior to Platelet-Rich Plasma or Hyaluronic Acid Alone in Inhibiting Inflammation and Improving Pain and Function. *Arthroscopy* 2021; 3: 903-915

Additional References

1. Fryar CD, Kruszon-Moran D, Gu Q, Ogden CL. Mean body weight, height, waist circumference, and body mass index among adults: United States, 1999-2000 through 2015-2016. *Natl Health Stat Report*. 2018.
2. Raphael IJ, Parmar M, Mehrganpour N, Sharkey PF, Parvizi J. Obesity and operative time in primary total joint arthroplasty. *J Knee Surg*. 2013. doi:10.1055/s-0033-1333663
3. Changulani M, Kalairajah Y, Peel T, Field RE. The relationship between obesity and the age at which hip and knee replacement is undertaken. *J Bone Jt Surg - Ser B*. 2008. doi:10.1302/0301-620X.90B3.19782
4. Liu B, Du Y, Wu Y, Snetselaar LG, Wallace RB, Bao W. Trends in obesity and adiposity measures by race or ethnicity among adults in the United States 2011-18: Population based study. *BMJ*. 2021. doi:10.1136/bmj.n365
5. Kohn MD, Sassoon AA, Fernando ND. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clin Orthop Relat Res*. 2016. doi:10.1007/s11999-016-4732-4
6. AAHKS, Position Statement. Biologics for Advanced Hip and Knee Arthritis Position of the American Association of Hip and Knee Surgeons. <https://www.aahks.org/position-statements/biologics-for-advanced-hip-and-knee-arthritis/>
7. Bennell KL, Paterson KL, Metcalf BR, et al. Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis: The RESTORE Randomized Clinical Trial. *JAMA*. 2021;326(20):2021–2030. doi:10.1001/jama.2021.19415
8. Kon, E., Di Matteo, B., Delgado, D., Cole, B. J., Dorotei, A., Dragoo, J. L., Filardo, G., Fortier, L. A., Giuffrida, A., Jo, C. H., Magalon, J., Malanga, G. A., Mishra, A., Nakamura, N., Rodeo, S. A., Sampson, S., & Sánchez, M. (2020). Platelet-rich plasma for the treatment of knee osteoarthritis: an expert opinion and proposal for a novel classification and coding system. *Expert opinion on biological therapy*, 20(12), 1447–1460. <https://doi.org/10.1080/14712598.2020.1798925>

Index: Patient Characteristics

PRP vs Placebo

In a double-blind RCT of 58 patients with Ahlback I-III unilateral or bilateral OA, where 31 knees were treated with 3 weekly injections of 2 ml leukocyte-poor PRP (RegenKit-THT, 1.8x platelets) and 27 knees with saline, the PRP group had higher PROs than saline at several time points (WOMAC score at all time points up to 12 months, and IKDC scores improved at six months) (REF Lin). In a cohort of 20 patients (63.3 years, 5M/15F, 24.1 BMI) with bilateral Ahlback I-II knee OA, each subject underwent randomized, blinded treatment in one knee with a single leukocyte-poor PRP (RegenKit-THT-1) injection while the contralateral knee received a 4 ml saline injection. Patient reported outcomes were improved for PRP vs saline; however, there was no improvement in the secondary outcome of the study, isokinetic strength testing (REF Wu). In a cohort of 102 patients with bilateral Ahlback I-II knee OA, 52 knees (53.1 years, 10/16 M/F, 26.3 BMI) received a single injection of 8 ml PRP (leukocyte filtered, 3x platelets), while 50 knees (51.6 years, 5/20 M/F, 25.8 BMI) received 2 PRP injections 3 weeks apart, and 46 knees (53.6 years, 6/17 M/F, 26.2 BMI) received one saline injection. Significant improvement was documented in PROs (both WOMAC and VAS pain scores) up to the 6-month follow-up evaluation in both PRP groups, without differences between 1 or 2 injections, while lower scores were noted in the saline group (Ref Patel). In a study of 20 patients with bilateral Kellgren-Lawrence 1-2 knee OA, 8ml of PRP (leukocyte-poor) was injected in one knee, and 8ml of saline injected in the contralateral. A significant improvement in PROs in the PRP knees when compared to the saline knees was found (WOMAC total score and VAS pain scores) up to the 6-months after injection (Ref: Ghai). In a study of patients with KL 1-3 OA (61.3 years, 1/29 M/F, 30.4 BMI), 30 patients received 3 injections of 4ml PRP (6x platelets, normal blood leukocyte values) and 27 patients (60.2 years, 3/24 M/F, 30.7 BMI) received one injection of saline (Elik). Significantly better PROs were found with PRP treatment (WOMAC, VAS pain, as well as quality of life) at time points up to 6 months. No improvement in cartilage thickness as measured with ultrasonography was found. In a cohort of 30 patients with KL 2-3 OA, 15 (53.5 years, 5/10 M/F, 29.5 BMI) received 3 weekly injections of 4 to 7 ml leukocyte poor PRP, while a similar amount of saline was administered in the other 15 patients (46.6 years, 6/9 M/F, 27.5 BMI). PROs were significantly in the PRP group (total WOMAC score) at time points up to 12 months (REF Smith). Two studies did not use the WOMAC scores to evaluate PRP and relied on different outcome measures. One study of 50 patients of patients affected by grade II-IV knee OA (60.0 years, 17/33 M/F, 29.7 BMI) received three weekly 5 ml PRP injections, while 50 patients (58.7 years, 20/30 M/F, 31.2 BMI) received three weekly saline injections. Pain scores improved significantly with PRP up to 6 months, while pain reduction was negligible for the saline group (Qamar et al). Another study evaluated two PRP (5x platelets and similar leukocyte values to whole blood) administration protocols vs saline in KL 1-4 knee OA patients treated blindly. One group of 44 patients (53.8 years, 19/25 M/F, 28.4 BMI) was treated with one injection of 5 ml PRP and 2 saline injections, one group of 39 patients (53.7 years, 16/23 M/F, 28.7 BMI) was treated with 3 weekly injections of PRP, and one group of 40 patients (52.8 years, 20/20 M/F, 29.5 BMI) was treated with 3 injections of saline. PRP led to better results vs placebo in terms of both IKDC subjective score and EQ-Vas score up to the 6-month follow-up. Moreover, their findings supported better results for the three-injection protocol, especially for early OA patients (Gomeli et al REF).

PRP versus prolotherapy

The high quality study (Rahimzadeh 2018) randomized 42 patients with KL grade 1-2 osteoarthritis in two groups with 21 on each side with mean age of 65.5 yr in prolotherapy and 64.3 yr in PRP group. The

moderate quality study (Eroglu 2016) randomly divided 60 patients with KL grade I-III OA in 3 groups with ending up 20 in prolotherapy group, 18 in PRP group and 20 in placebo group with mean age respectively 66 yr, 64.16 and 62 yr. Pre-injection demographics including age, gender, BMI and pre-injection score were similar in all groups in both studies except female predominance in all 3 groups in Eroglu study.

Rahimzadeh et al had performed total two injections in each group one month apart with one group receiving 7 ml PRP and other group 7 ml of dextrose 25%. Eroglu had performed total 3 injections 3 weeks apart in each group: dextrose 6 ml intraarticular injection in prolotherapy group, 6 ml PRP activated with 10% added calcium chloride in PRP group and 0.09% of NaCl in placebo group.

The patients were clinically evaluated at four points of time in Rahimzadeh study: pre-injection, one month (one month from 1st injection), second month (one month from second injection), and 6 months follow up while total 5 times in Eroglu study (baseline, before 2nd injection (3 weeks after first injection), before 3rd injection (6 weeks from 1st injection), 3 months and 6 months.

On follow up evaluation Rahimzadeh et al found clinically significant improvement in physical activity (functional limitation), pain scores, stiffness score and WOMAC scores in both groups. The improvement process had an upward trend for up to 8 weeks after the intervention, and the maximum improvement was observed in that period; thereafter, there was a slight but nonsignificant decline in scores until Week 24. They attributed this decline in scores to overuse of the knee from pain relief and improved function. The comparison of two groups in similar time sessions was statistically significant in the second and sixth months which demonstrated better results for PRP; and not significant at pretreatment and in the first month, for physical activity, pain scores and WOMAC scores, which they attributed to similar scores between the groups at months 0 and 1. All pair comparison at different time periods in both groups were clinically significant for physical activity, pain scores, stiffness scores and WOMAC scores. They were not significant for stiffness scores at 1st vs 6th and 2nd vs 6th months. The main effect of time and interaction of time with treatment group while using mixed-model ANOVA, was statistically significant for physical activity, pain scores, and WOMAC score whereas the P-value of the main effect of the treatment group was borderline which they attributed to similar scores at 0 and 1 month. On the contrary, Eroglu et al found no significant difference between the groups in terms of total and subscale WOMAC scores though there was nonsignificant increase in scores in prolotherapy and PRP groups. There were limitations of both studies though one was high and one moderate quality. They had small sample size and short term follow-up. Eroglu et al did not have blinding, no priority analysis, female predominance and included grade 3 KL grade in their studies which involves higher-grade damage in the joint.